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The Effects of Disease Activity, Sleep and Depressive Symptoms on Fatigue in Systemic Lupus Erythematosus

by

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A dissertation submitted to the Graduate Faculty in Psychology in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

The City University of New York

1998

UMI Number: 9820563

[1] Chapter 2 has been published as:
McKinley, P. S., Ouellette, S. C., & Winkel, G. S. (1995). The contributions of disease activity, sleep patterns, and depression to fatigue in systemic lupus erythematosus: A proposed model. *Arthritis & Rheumatism, 38*(6), 826-834. © 1995 by the American College of Rheumatology. Reprinted with permission of Lippincott-Raven Publishers.

This manuscript has been read and accepted for the Graduate Faculty in Psychology in satisfaction of the dissertation requirement for the degree of Doctor of Philosophy.

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Abstract

The Effects of Disease Activity, Sleep and Depressive Symptoms

on Fatigue in Systemic Lupus Erythematosus

by

Paula S. McKinley

Advisor: Professor Arthur J. Spielman

A majority of people with systemic lupus erythematosus consider fatigue their most debilitating symptom, yet its etiology is unknown. The purpose of this dissertation is to redefine the subjective fatigue concept into more meaningful components. Two approaches are used. Results from a cross-sectional study and a two-week daily diary study are presented. Participants were women with lupus. A comparison group of women without lupus was recruited through acquaintance referrals.

First, the lived experience of fatigue phenomenology and time course is explored. Fatigue dimensions, including sensations, perceptions, chronicity, affective attributions and functional consequences of fatigue, are described. For women with lupus, negative affective appraisals of fatigue and its perceived functional impact are higher than for women without lupus. Physical and cognitive fatigue phenomenology, conversely, are not distinctive. In terms of daily time course, fatigue fluctuates within days and across days in a cyclical, ebb and flow pattern. Women with lupus consistently report higher fatigue during the day, but not at bedtime, than their peers. In retrospective estimates and a daily sleep log, women with lupus report poorer quality, more disrupted sleep despite longer nightly time in bed. Depressive mood was not different between the groups in either cross-sectional or daily ratings.

The second approach to defining lupus fatigue is to test a multifactoral, mediational explanatory model of fatigue. The model posits that lupus disease activity, decreased sleep quality, and depressive symptoms and mood all affect lupus fatigue, but not as independent factors. The results support a model in which sleep and mood can be mediators or mechanisms through which disease activity increases fatigue. Further, poor sleep and depressive mood can help perpetuate each other through a reciprocal causal process. The model was generally supported with both cross-sectional and daily data. This model redefines fatigue as the end product of several underlying factors that affect fatigue through their ongoing relationships to each other. This model is not purported to be a comprehensive etiological model. Instead, its value is in identifying viable intervention strategies for fatigue. The results suggest that existing, nonpharmacological interventions for sleep and mood disturbance may help alleviate lupus fatigue.

Acknowledgments

I was preparing to print the final draft of this dissertation the day before it was due in the committee's hands. It was a Sunday, and I learned the university's computer network server had crashed. Dan, a colleague and fellow Ph.D. from my part-time job, rescued the day by loaning me his personal laser printer. As John, my friend of friends, drove me to pick up the printer, I had an epiphany about the obvious. "It takes a lot of people to do a dissertation," I said. Indeed, many people have given me love, support, mentoring, advice, collaboration and example which have in some way contributed to this accomplishment. I can thank only a few of them here.

The mentoring of my diverse, multidisciplinary thesis committee made it possible to cover the broad theoretical ground I attempted in this dissertation. Prof. Art Spielman, as the committee chair, provided crucial design and methodology advice, and clinical insights in interpreting the sleep data. Prof. Gary Winkel invested countless hours to insure that I addressed the difficult questions posed in these studies with the best possible data analytic approaches. His enthusiasm for my work was critical at times when mine waned. Prof. Suzanne Ouellette has been a mentor and friend for much of my graduate school tenure. Through my work on her research studies, her role in establishing the Health Psychology Concentration, and her enduring faith in me, she provided a forum for me to carve out a unique, eclectic training path.

The external readers on the committee contributed far beyond their role. Prof. Howard Tennen accepted this role with raw enthusiasm. His open, friendly style made me instantly receptive to his long list of focused, insightful comments, which will be invaluable as I prepare these chapters for publication. Dr. Stephen Paget was a crucial collaborator in recruiting participants for the studies and providing a clinical perspective on many aspects of the work. He has enthusiastically supported my involvement in the interdisciplinary research activities facilitated by the Cornell Arthritis and Musculoskeletal Diseases Center (MAC). All the members of the MAC's ongoing research methodology group have acted as both consultants and cheerleaders from design to completion of this research. Prof. Tracey Revenson, through her roles in the Health Psychology Concentration and the MAC has been my de facto committee member, mentor, advisor, friend, and professional role model for many years.

Research like this absolutely depends on two things: participants and funding. I thank the women with lupus and their acquaintances who gave their time to these studies. I am grateful to have met many of them in person. I also thank the physicians who helped put me in contact with their patients and completed questionnaires in the midst of their busy schedules. Funding by the National Arthritis Foundation, the New York City Arthritis Foundation and an NIMH National Research Service Award training grant to the CUNY Health Psychology Concentration supported my time and the materials needed to complete the large, daily diary study. I also thank Casio Corporation for donating alarm watches used in the daily diary study.

I owe the deepest gratitude and my daily well being to John, Sandra, Hilary, Chris and Matthew — the Zucchinis, a moniker for our small clan. They are my colleagues, friends, neighbors, family and hunter-gatherer camping buddies. The following quote, about a fiction-writing support group, describes us well:

> " . . . one of those weird little families we fashion out of whoever's around us. They're very tender with one another. All four of them are excellent writers, but only one of them has been published at all, and that was just one article. But you know what? They love each other. They still look forward to their meetings after all these years. They all look a lot less slick and cool than they did when they were in my class, because helping each other has made their hearts get bigger. A big heart is both a clunky and a delicate thing; it doesn't protect itself and it doesn't hide. It stands out, like a baby's fontanel, where you can see the soul pulse through. You can see this pulse in them now." — Anne Lamott, *bird by bird*

Other friends and colleagues who provided support, empathy, a social life, and critically timed free meals include Emily, Patricia, Susan, Bonnie, Jamie, Beth, Alison, Edwin, Beth, and Josie, and the whole Graduate Center gang. Special thanks to Kathleen and Joanne who lived in close proximity through the design and implementation of this research.

Friends and family in Arkansas have encouraged me from afar, even though I defected to another planet — New York. I thank especially my brother Freddie, cousins Darrellyn and Sherry, Alan, Lori, and my adopted family, the Wards and Jones'.

One of life's amazing gifts is having good parents. Mine have been loving, supportive, and unwavering in their faith in me throughout all my efforts in life, including this seemingly infinite degree process.

Ok, so I thanked many people, after all. They all deserve it.

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Chapter 1

Overview

People living with systemic lupus erythematosus (lupus) must contend with a variety of symptoms and potentially severe complications which arise in an unpredictable disease course. Fatigue might be expected to be relatively benign in this context; nevertheless, a majority of people with lupus consider fatigue their most debilitating symptom. Descriptive studies and clinical anecdotes suggest that fatigue limits participation in valued activities through its chronic, unpredictable impact on daily functioning. While it is often not the most severe manifestation people with lupus experience, ongoing fatigue may erode one's sense of vitality and satisfaction in important quality of life arenas.

The etiology of lupus fatigue is unknown. Lupus' pathophysiology likely contributes to fatigue, and various mechanisms are being explored. Currently, however, fatigue is considered a nonspecific lupus symptom. It arises under a range of disease states and severity, rather than being correlated with particular disease pathology or symptoms. Fatigue is a ubiquitous problem in a variety of conditions and populations. Increasingly, researchers in various disciplines recognize that fatigue is likely a complex phenomenon affected by psychological, social and cultural, as well as physiological factors. There is a growing consensus among rheumatology researchers and clinicians that lupus fatigue arises from a multifactoral etiology. Researchers have begun investigating psychophysiological, psychological and behavioral factors that may contribute to lupus fatigue. Pain, sleep pathology, depression or depressive symptoms, and lack of aerobic fitness have been correlated with fatigue in lupus or other rheumatic disease groups. This is a promising line of research because such factors offer potential avenues for fatigue interventions. Most research on fatigue in rheumatic disease populations defines and measures fatigue as a unitary construct. Further, most studies have not involved a multifactoral approach to etiological questions about fatigue.

Clinical experience and a growing literature in various populations suggest that "fatigue" may better be seen as a heuristic for a multidimensional phenomenon. Fatigue may be experienced in a variety of ways and may arise from numerous etiological pathways. The purpose of this dissertation is to refine the definition of lupus fatigue by deconstructing the layperson's subjective fatigue concept into more meaningful components. Two approaches are used in this effort. First, the lived experience of fatigue, in terms of both phenomenology and course over time, is described. A multidimensional fatigue measure is used to describe the sensations, perceptions, chronicity, affective attributions and functional consequences of fatigue. The results indicate that fatigue is not a unitary experience. For women with lupus, the experience of fatigue is distinguished from fatigue experienced by their peers in terms of its functional impact and the women's affective attributions about fatigue. The physical and cognitive phenomenology of fatigue, on the other hand, may not be so distinctive for people with lupus.

The short-term time course of fatigue is investigated for fourteen days with a daily events methodology. Fatigue is a difficult symptom to explain and to manage. Prevalence estimates and anecdotal fatigue descriptions suggest that fatigue occurs chronically in the course of everyday activities more than in acute, discrete episodes. A few studies in other rheumatic disease populations have shown that pain, fatigue and mood fluctuate daily and may be causally related, but there have been no studies of daily fatigue in lupus. Among women with lupus in the studies presented here, fatigue does fluctuate both within days and across days in a cyclical, ebb and flow pattern. Compared to their peers, women with lupus report higher fatigue during the day but not at bedtime. These results suggest that a daily level of analysis is important for identifying clinically relevant fatigue fluctuations among people with lupus. Through these two types of descriptive data, lupus fatigue is redefined as a multidimensional experience whose daily fluctuations may explain the debilitating impact of fatigue people with lupus have reported in other studies.

The second approach to defining lupus fatigue is to propose and test a multifactoral explanatory model of fatigue. I propose that fatigue is a product of biomedical, psychophysiological and psychological factors which are operationalized, respectively, as lupus disease manifestations; decreased sleep quantity and quality; and depressive symptoms and mood. These three factors are not proposed as independent causes of fatigue; rather, sleep and mood are proposed to be mediators or mechanisms through which disease activity increases fatigue. More specifically I propose that poor sleep and depressive mood help perpetuate each other through a reciprocal causal process, and that this process is a mediational mechanism through which lupus disease manifestations contribute to fatigue. This model redefines fatigue as the end product of several underlying factors that affect fatigue through their ongoing relationships to each other. This model is not purported to be a comprehensive etiological model. Instead, the value of this particular model is identifying viable intervention strategies for fatigue. Using both cross-sectional and prospective, daily data, this model is generally supported. The results suggest that existing, nonpharmacological interventions for sleep and mood disturbance may help alleviate fatigue.

Organization of the dissertation. Results from two studies comprise this dissertation. The results are presented here in a somewhat nonstandard dissertation format. Chapters 2 through 4 present results from the two studies in the form of three papers written in standard American Psychological Association journal manuscript format. The papers are written as articles that can stand alone, although each article sometimes refers the reader to findings presented in one of the other articles. The reference lists, tables and figures appear with their respective chapters. In keeping with standard dissertation format, there is also a bibliography listing the references from all chapters at the end of the dissertation.

Chapter 2

The Contributions of Disease Activity, Sleep Patterns and Depression to Fatigue in Systemic Lupus Erythematosus: A Proposed Model [1]

For those living with systemic lupus erythematosus (lupus), the disease's potential variety and severity of manifestations (Liang, Socher, Larson, & Schur, 1989), and unpredictable flare-and-remit course create challenges and repercussions in all arenas of life. In this context, fatigue might be assumed relatively benign, yet it is often one of the most debilitating symptoms (Krupp, LaRocca, Muir, & Steinberg, 1990; Liang et al., 1984; McCoy, Callahan, & Pincus, 1992; Robb-Nicholson et al., 1989). During pilot interviews for a six-month prospective study of stress and its effects among women with lupus (hereafter, the Lupus Stress Study; see Note 1), many women talked about fatigue, evoking three themes (Ouellette, Bochnak, & McKinley, 1989). First, the women presented fatigue as restricting their daily lives by affecting both home and work involvements. Second, they diligently attempted to get "enough" rest and sleep to control fatigue and other symptoms. Finally, rest and sleep were often futile in alleviating fatigue.

A program of research on lupus fatigue has been undertaken, with data from the first study reported here. The purposes of this paper are to provide descriptive data about the nature of lupus fatigue, and to introduce a multivariate model addressing the impact of sleep problems and depression, as well as disease activity, on lupus fatigue.

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1 This chapter has been published as:
McKinley, P. S., Ouellette, S. C., & Winkel, G. S. (1995). The contributions of disease activity, sleep patterns, and depression to fatigue in systemic lupus erythematosus: A proposed model. *Arthritis & Rheumatism, 38*(6), 826-834. © 1995 by the American College of Rheumatology. Reprinted with permission of Lippincott-Raven Publishers.

The etiology of lupus fatigue is not well elaborated. Disease activity is typically considered a primary, direct cause (Liang et al., 1989); however, between disease flares, when pathophysiological processes are less active, fatigue can be an enduring problem. We propose that, in addition to disease activity, sleep problems and depression are likely contributors to fatigue. These three factors, however, are not expected to be independent causes of fatigue. Rather, we propose that sleep problems and depression are mediators or mechanisms through which disease activity increases fatigue. Our proposed model of these processes is shown in Figure 1.

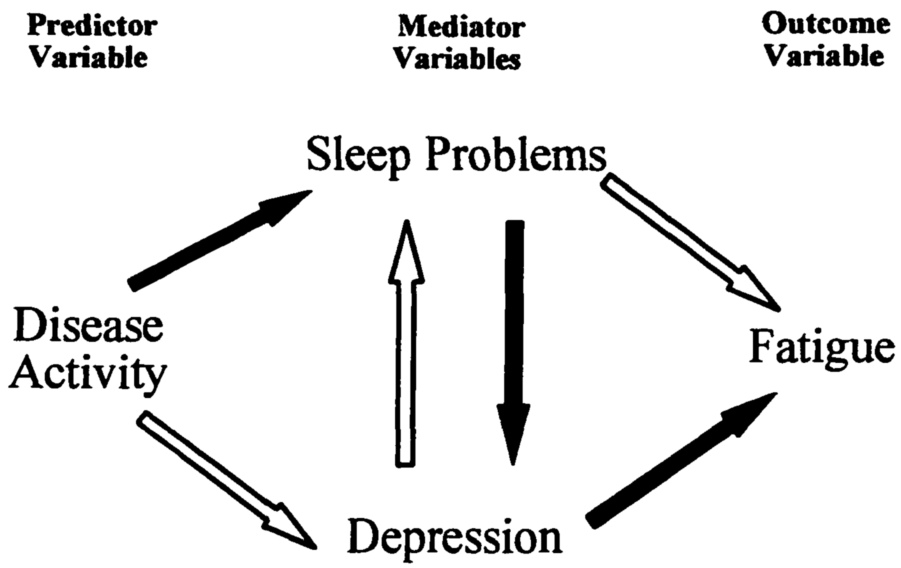

Figure 1. Proposed model of lupus fatigue. The effects of lupus disease activity on fatigue are mediated by both sleep problems and depression. In the Disease → Sleep → Depression pathway, depression is the most proximal cause of fatigue. In the Disease → Depression → Sleep pathway, sleep problems are the most proximal cause. Finally, sleep and depression are proposed to affect each other in a reciprocal feedback-type relationship. Regardless of which mediator is found to be the most proximal link with fatigue, this reciprocal relationship may allow both sleep and depression to have significant effects on lupus fatigue.

Sleep Problems

Disease
Activity

Fatigue

Depression

Figure 1. Proposed model of lupus fatigue. The effects of lupus disease
activ

People with sleep disorders or experimentally induced sleep disruption experience a great deal of daytime sleepiness and fatigue (Bonnet, 1985; Spielman, Saskin, & Thorpy, 1987; Stepanski, Lamphere, Badia, Zorick, & Roth, 1984; Sugerman, Stern, & Walsh, 1985). Sleep fragmentation is exhibited in several types of rheumatic diseases exhibit sleep fragmentation (Hirsh et al., 1994; Mahowald, Mahowald, Bundlie, & Ytterberg, 1989; Moldofsky, Lue, & Saskin, 1987; Moldofsky, Lue, & Smythe, 1983; Moldofsky, Scarisbrick, England, & Smythe, 1975), and can be correlated with disease symptoms and levels of fatigue (Mahowald et al., 1989; Moldofsky et al., 1987; Moldofsky et al., 1983; Moldofsky et al., 1975). Given the degree to which fatigue is a problem for people with lupus, sleep is likely also to be a problem. Symptoms such as pain and fever or medication side effects may cause restless sleep. Disease symptoms may also lead to sleeping more or staying in bed longer in an, often unsuccessful, attempt to sleep. It was reported that before an aerobic conditioning program, a majority of women with lupus experienced sleep disturbance (61%) and fatigue (74%) (Robb-Nicholson et al., 1989). Many of them (70%) tried to manage their fatigue with rest. After eight weeks of exercise, aerobic fitness had improved, and fatigue had decreased. Collectively these findings demonstrate that sleep disruption or loss, as well as too much rest and sleep, can exacerbate fatigue. Effective strategies for alleviating fatigue may include, paradoxically, getting less sleep in the service of improving sleep quality (Spielman et al., 1987), and increasing activity (Robb-Nicholson et al., 1989).

Symptoms of depression have been reported by 39–42% of people with lupus (Krupp et al., 1990; Liang et al., 1984; Robb-Nicholson et al., 1989). When disease symptoms worsen, depression may be more likely to occur or worsen. At such times it is often more difficult to cope with both the illness and other aspects of life. Thus, the physical lethargy and cognitive sluggishness that are often symptomatic of depression may be reported, by health care providers and patients as "fatigue".

There is a widely recognized link between sleep pathology and depression (Reynolds & Kupfer, 1987; Van den Hoofdakker & Beersma, 1988). The causal direction of this link is uncertain: Does sleep pathology lead to depression, or does depression lead to sleep pathology? In the case of lupus, the *initial* causal direction may be not only elusive, but also less relevant than understanding the ongoing link throughout the flare-and-remit course of the illness. Our model proposes that sleep problems and depression help perpetuate each other through a reciprocal causal process, and that this process is a mediational mechanism through which lupus disease activity causes fatigue.

These proposed relationships are conceptualized as two possible pathways leading to fatigue. In both, sleep and depression mediate the effects of disease activity on fatigue. the Disease –> Sleep –> Depression path (Figure 1, filled arrows) predicts that depression is the most proximal causal link to fatigue, whereas the Disease –> Depression –> Sleep path (Figure 1, open arrows) points to sleep as the proximal cause. Including both pathways in the model accounts for the proposed reciprocal causation between sleep and depression.

Fatigue Study data were collected in conjunction with a six-month Lupus Stress Study (Note 1), in which participants were already enrolled. Only results from the first of six interviews are reported here.

Method

Participants

Women with lupus. Women between the ages of 18 and 65 who had lupus, as confirmed by their rheumatologists using the American Rheumatism Association criteria, (Tan et al., 1982) were recruited from the patient registry of the Hospital for Special Surgery, New York, NY, which specializes in rheumatic and musculoskeletal diseases. Of 64 women completing the first interview, only 54 received the Fatigue Study measures because fatigue data collection began after the Stress Study was underway. Six patients were excluded due to missing data (> 25% of all items). All data reported here are from the remaining 48 women.

Participants' ages were 22 to 64 years (mean = 35.17). Median education was college graduate (4 yrs college), and median household income was $40,000 - $49,000. While the majority (59.6%) were white and of European descent, a sizable proportion (40.4%) were women of color, including African Americans (17%), Latin Americans (14.9%), and Asian Americans, Pacific Islanders or Native Americans (8.5%). A majority (56.3%) were working outside the home. Most were married or living with a partner (54.2%) or involved in a romantic relationship (16.6%). The others were separated, divorced or never married (29.2%). A total of 43.8% had at least one child, but most (56.3%) had no children (range = 0 - 3 children).

Comparison group. For a comparison group, our interest was in comparing the experiences of women with lupus to a general population, rather than to an atypically healthy population. Lupus group participants were asked to provide names of female acquaintances who "did not have lupus" and were demographically similar to themselves.

Thirty-three comparison group participants were recruited from this pool. Of these, 27 returned valid data (< 25% missing values) for the Fatigue Study measures.

Compared with the lupus group the comparison group was slightly older (mean = 42.19 yrs; range 25 - 60 yrs) and had a similar median educational level (4 yrs college); a larger proportion of white women (78.6%), and a larger proportion who were working outside the home (88.9%). Their median household income was higher ($60,000 - $79,000), relationship status similar (66.6% married/living together; 3.7% serious relationship; 29.6% separated/divorced/never married), and a larger proportion had at least one child (81.5%; range = 0 - 6 children). The difference in work status between the groups may account partly for the difference in income level.

As expected, the comparison group's health status varied somewhat. Most women rated their overall current health as “excellent” or “good” (85.2%), but three (11.1%) said “fair”, and one (3.7%) rated her health as “poor”. From a checklist of current or past health problems, the most frequent were allergies (40.7%), chronic back pain (29.6%), skin disorders (25.9%), and gynecologic disorders (22.2%). The four women rating their health as “fair to poor” listed some of the following as current health problems: 1) chronic back pain (from injury), allergies, and gynecologic problems; 2) joint disorder (hip problems due to running), depression, allergies, acne; 3) retinitis pigmentosa, allergies; 4) rheumatoid arthritis (RA), high blood pressure, high white blood cell count, chronic back pain, gastrointestinal disorder (not specified), and allergies. Two of these four (7.4% of comparison group) were the only ones in the group to say their current health was “worse” compared to six months ago.

One other woman reported having RA, along with chronic back pain, sleep problems (not specified), and allergies; however, she rated her current health as "good". No one reported other rheumatologic disorders or conditions associated with such disorders, even though conditions such as Sjogren's syndrome, Raynaud's syndrome, scleroderma and kidney disease were included on the checklist.

Measures

Fatigue. The fatigue measure was chosen based on a multidimensional definition of fatigue as a subjective sense of tiredness, lack of energy or a decreased capacity for performing one's usual physical or mental activities. The Piper Fatigue Scale (PFS) was developed by a nursing researcher based on clinical experience and fatigue descriptions in the literature (Piper et al., 1989). There are 40 items comprising four subscales; answers are given on a 100 mm visual analog scale (VAS). Each subscale is scored as the mean of its items, allowing a possible range of 0 (low fatigue and "desirable" attributes) to 100 (high fatigue and "undesirable" attributes) (Piper, 1989b).

The PFS *Temporal* subscale (4 items) assesses the time course of fatigue with an emphasis on chronicity: level of fatigue "now"; whether current fatigue is continuous vs. intermittent; chronic vs. acute; and the degree of fatigue increase or decrease in the past week. Internal consistency reliability for this subscale was good ($\alpha = 0.75$). The *Severity* subscale (12 items) includes items such as: fatigue severity "now"; the degree that fatigue is interfering with household cleaning, work, reading, social activities, sex, etc. Scale reliability was very good ($\alpha = 0.95$). The *Affective* subscale (5 items) is designed to tap the "emotional meaning of fatigue" (Piper et al., 1989). Items assess whether fatigue is perceived as: negative vs. positive; abnormal vs. normal; unpleasant vs. pleasant;

destructive vs. protective; and disagreeable vs. agreeable. Scale reliability was very good ($\alpha = 0.95$). The *Sensory* subscale (19 items) assesses experiences that may be associated with or attributable to fatigue. Items include physical sensations (strong vs. weak), motivations (bored vs. interested), emotions (sad vs. happy) and cognitive functions (unable vs. able to concentrate). Scale reliability was very good ($\alpha = 0.94$). Following Piper's scoring instructions, an *Overall Fatigue* score was obtained from the mean of these four subscale scores (Piper, 1989b).

There are no published normative data for the PFS, but Piper has reported PFS scores for women with breast cancer receiving chemotherapy (Piper, 1992). A series of *t* tests were performed comparing our sample's PFS scores to Piper's sample at two times in the chemotherapy study: before women's first chemotherapy cycle, and after their third of six cycles (highest PFS scores reported in that study). There were no significant differences, which demonstrates that fatigue on the PFS is comparable between women with lupus and other clinical populations.

Disease activity and severity. Each woman's rheumatologist completed the Systemic Lupus Activity Measure (SLAM) (Liang et al., 1989). On a graded scale from "absent or normal" to "severe", a physician rates the most severe occurrence of 24 lupus symptoms during the previous month, as well as 8 laboratory measures. Ratings are summed into an index of the severity of "current disease activity". The SLAM has high convergent validity with five other lupus disease activity measures ($r = 0.901$) and high inter-rater reliability ($r = 0.861$) (Liang et al., 1989).

For this study the single fatigue item (item 2) was removed from the SLAM score to avoid confounding of disease activity with fatigue. Scale reliability for the corrected SLAM score, hereafter called SLAM-F, was only moderately high (α = 0 .62), but it was not different from the reliability of the uncorrected SLAM scores (α = 0.66). Normative scale reliabilities have not been published. Our sample's SLAM scores were lower than those of the SLAM validity study sample (Liang et al., 1989) (mean = 5.31 vs. 7.71, t (71) = -2.128, $p < 0.05$). Several participants with higher SLAM scores had to be excluded because of disease flares or cognitive impairments associated with lupus.

Sleep. The Sleep Symptom Questionnaire (SSQ) is a self-report scale assessing sleep quantity and quality indicators common to insomnia (Spielman, 1990). Ten items assess symptom frequency in the past week on a scale from 1 = "never" to 5 = "always". On two other items, participants estimated their nightly total sleep time (TST) and sleep onset latency (SLAT) for the past week to assess sleep quantity and sleep disruption as a sleep initiation problem.

While sleep self-reports are not as quantitatively accurate as polysomnographic measures, the two methods are usually well correlated for measures of TST and SLAT in people with no sleep complaints (Hoch et al., 1987) (r = 0.63 to 0.82) and in people with insomnia (Frankel, Coursey, Buchbinder, & Snyder, 1976; Spielman et al., 1987) (r = 0.64 to 0.84). In a recent study people with RA tended to underestimate polysomnogram-recorded sleep latency (20.4 vs. 28 mins) and nighttime awakenings (3.7 vs. 21.3) but were fairly accurate in estimating total sleep time (408.9 vs. 406.8 mins) (Hirsh et al., 1994). Such findings suggest our resulting self-reports may provide a conservative estimate of sleep problems among women with lupus.

Because the SSQ has not been standardized, exploratory factor analyses were performed on the ten scaled items and the SLAT and TST estimates. A five-factor, oblique rotation was chosen as the best solution. Two of the five factors were most directly relevant to the proposed fatigue model: 1) a *sleep disruption* factor, assessing actual sleep disturbances and loss, including restless or disrupted nighttime sleep and sleep latency (SLAT); and 2) a *sleep anxiety* factor, asking about lying awake feeling anxious, worrying about sleep or watching the clock, and worrying about nighttime sleep during the day. These two factors were moderately correlated ($r = 0.46$). Factor scores generated by the SPSS Factor procedure (SPSS, 1994) were used in analyses testing the fatigue model.

Depression. The Center for Epidemiological Studies Depression scale (CESD) (Radloff, 1977) has been a useful index with rheumatic disease populations, but Blalock and colleagues (Blalock, DeVellis, Brown, & Wallston, 1989) demonstrated that four of the twenty items (items 7, 8, 11 & 20) can inflate the incidence and severity of depression in an RA population. Three of these items are face-valid indicators of sleep disruption and fatigue, so the four "arthritis biased" items were removed. The sum of the remaining sixteen items was multiplied by a constant of 1.25 to retain the original 0-60 range (Blalock et al., 1989). Reliability of this modified measure (CESD-AR) was good ($\alpha = 0.89$)

Procedure

For the Lupus Stress Study (Note 1), participants completed a semi-structured interview and a written questionnaire which included the Fatigue Study measures. Lupus participants' interviews were typically conducted the same day as, and not later than three months after a targeted examination by their rheumatologist, who was asked to rate the SLAM based on observations and laboratory results obtained on the targeted examination date. This procedure ensured that the SLAM disease activity ratings were current with the interview data.

Between groups analyses. Data from the lupus and comparison groups were compared with Hotelling's T^2 statistic using the SPSS software's MANOVA procedure. In separate analyses the groups were compared on the following dependent variables: 1) four PFS subscale scores; and 2) three sleep measures (SSQ, TST, and SLAT). Post hoc univariate tests were used to determine which specific dependent variables were significantly different between the groups. One-way analysis of variance was used to compare the groups' mean overall PFS score (mean of four subscales) and CESD-AR score.

Statistical test of fatigue model. Using only data from the lupus group, the variables used to test the fatigue model (Fig. 1) were: Disease Activity during the previous month (SLAM-F), Sleep during the previous week (separate analyses using Sleep Disruption and Sleep Anxiety factor scores), Depression ratings during the previous week (CESD-AR) and Fatigue "right now" (PFS). Because of high PFS subscale intercorrelations, the overall PFS score was used.

The first step in determining mediator effects requires testing the relevant direct effects with univariate regression equations (Baron & Kenny, 1986). These direct pathways are implicit but not all are illustrated in Fig. 1. Specifically, the predictor variable (Disease Activity) and both mediators (Sleep and Depression) should directly affect the outcome variable (Fatigue); the predictor should affect both mediators; and because Sleep and Depression are proposed to mediate each other's effects on Fatigue, Sleep should predict Depression, and Depression should predict Sleep. If such direct relationships are not confirmed, it is statistically and logically impossible for mediational effects to occur. For instance, if disease activity does not affect fatigue, sleep disruption cannot be the mediator (i.e., mechanism of action) explaining this nonexistent effect. In eleven univariate regression equations these direct effects were confirmed, although the SLAM-F was a weak predictor of the CESD-AR ($R^2 = 0.049$, $p = 0.14$) and Sleep Anxiety ($R^2 = 0.042$, $p = 0.17$).

The next analysis step employed two-stage least squares regression (2SLS), a type of structural equation modeling (James & Singh, 1978), to test the mediational pathways in the model. Unlike regular least squares regression, 2SLS regression allows simultaneous estimation of several equations, thus providing a means of testing reciprocal causation between two variables. This is precisely the situation proposed with regard to the effects of sleep and depression on fatigue. We used the SYSREG procedure available in the SAS ETS module. It should be noted that general multiple regression programs in most software packages will not perform this type of regression. Using 2SLS, all predicted and error variances for the two paths in Fig. 1 were estimated simultaneously for a *system* of three regression equations. These equations mirror the paths illustrated in Fig. 1 and are specified in Tables 1 and 2. The order of entry of variables into the equations was not specified. More complete explanations of the procedures required for two-stage regression are offered by James and Singh (James & Singh, 1978); Duncan (Duncan, 1975); and Judd and Kenny (Judd & Kenny, 1981).

Confirmation of the hypothesized model is obtained if the results take the following form: In equation 1, Sleep is the only significant predictor of Depression, reducing or nullifying the effects of Disease activity on Depression found in a univariate regression. This confirms that the effect of Disease Activity on Depression takes place through the mechanism of Sleep. Similarly in equation 2, Depression is the only significant predictor, mediating between Disease Activity and Sleep. Looking across both equations, reciprocal causation is confirmed if Sleep predicts Depression *and* Depression predicts Sleep. Finally, equation 3, the same for both paths, tests whether both Sleep and Depression mediate the effects of Disease Activity on Fatigue. The full model is confirmed if Disease Activity is nonsignificant, while both Sleep and Depression are significant predictors of Fatigue.

Results

Between-groups differences. On the PFS the lupus group reported a higher Overall Fatigue score in a univariate comparison (F (1,73) = 5.21, p = 0.03). The multivariate test of the PFS subscales revealed a marginally significant trend (Note 2) for the lupus group to report higher fatigue scores (F (4,69) = 2.05, p = 0.098). Post hoc univariate F tests revealed higher scores on the Temporal (F (1,72) = 6.42, p = 0.013) and Affective (F(1,72) = 6.33, p = 0.014) fatigue subscales, and a trend for higher fatigue Severity scores (F(1,72) = 2.71, p = 0.104). In neither group were Severity scores very high, however (means: Lupus = 29.05 vs. Comparison = 20.98). There was no difference on Sensory aspects of fatigue (F (1,72) = 1.46, p = .230).

In a multivariate test of the three sleep variables (SSQ, TST, SLAT), the lupus group reported greater overall problems with sleep (F (3,66) = 4.76, p = 0.005). Univariate post hoc tests revealed this difference was primarily due to longer sleep latency (mean = 49.38 vs. 20.36 mins; F (1,68) = 6.38, p = 0.014). There were trends for the lupus group to get more total nightly sleep (mean = 443.27 vs. 402.96 mins; F(1,68) = 3.26, p = 0.075), and to report greater sleep problems on the SSQ (ten scaled items) (F(1,68) = 2.23, p = 0.140). Within individuals, TST and SLAT were not well correlated (r = 0.195, p > 0.05); these findings thus seem to represent distinct trends throughout the group.

In a univariate *F* test the lupus group tended to score higher on the CESD-AR, but not significantly so (mean = 15.58 vs. 12.54; $F(1,73) = 1.43$, $p = 0.236$). In spite of this lack of difference, 50% of the lupus group scored ≥ 16, the standard cutoff representing clinically significant levels of depression on the CESD (Radloff, 1977).

Fatigue model results. Tables 1 and 2 present results of the 2SLS analyses of the model using the Sleep Disruption and Sleep Anxiety factor scores, respectively. In the tables unstandardized beta weights indicate the unit change in the outcome variable effected by the predictor, providing a relative index of the effect's strength. The value needed to reach statistical significance of unstandardized beta weights may change across equations. The variable order presented here corresponds to Figure 1. For equation 3 the variable order corresponds to the pathway which received stronger statistical support. The overall R^2 value indicates the total percentage of outcome variance accounted for by the system of three equations.

Results with Sleep Disruption factor. Equation 1 in Table 1 shows that Sleep Disruption, rather than Disease Activity, significantly predicted Depression, confirming that Sleep Disruption mediates between Disease Activity and Depression. Likewise in equation 2, Depression mediated the effects of Disease Activity on Sleep Disruption. A reciprocal relationship between Sleep Disruption and Depression was confirmed by the significant effects in both directions in both equations. Finally in equation 3, Disease Activity did not signficantly predict Fatigue. Depression was a marginally significant predictor of Fatigue, but the beta weight indicates its effect was weak. Sleep Disruption had a significant, strong effect on Fatigue. The effects of Disease Activity on Fatigue, therefore, were mediated somewhat by Depression and, to a much greater degree, by Sleep Disruption.

In this model Sleep Disruption had the most proximal effect on Fatigue. Disease Activity and Depression, through the reciprocal relationship of Depression with Sleep Disruption, had more distal effects. In summary, when the Sleep Disruption factor was used as the measure of sleep problems, the Disease --> Depression --> Sleep pathway leading to fatigue received stronger support than the other pathway.

Table 1. Two-stage regression analysis of fatigue model using sleep disruption as the measure of sleep

Equation	Predictor Variable	b_p	Mediator 1	b_{m1}	Mediator 2	b_{m2}	Outcome Variable
1	Disease Activity	0.55	Sleep Disruption	6.43**			Depression
2	Disease Activity	0.03	Depression	0.06**			Sleep Disruption
3	Disease Activity	0.73	Depression	0.36†	Sleep Disruption	7.44**	Fatigue

Overall R^2 for the 3-equation system = 0.48

**p < .01 *p < .05 †p < .15

Results with Sleep Anxiety factor. Using the Sleep Anxiety factor (Table 2) the results were slightly different but suggested the same conclusion. In equation 1, both Disease Activity and Sleep Anxiety had independent, significant effects on Depression, so there is no mediational effect. In equation 2, however, Depression did mediate the effects of Disease Activity on Sleep Anxiety. Looking across equations 1 and 2, a reciprocal relationship between Sleep Anxiety and Depression was confirmed. In equation 3 Disease Activity was not significant. Sleep Anxiety and Depression both predicted Fatigue, but Sleep Anxiety had a much stronger effect, while Depression was only marginally significant ($p < 0.15$). In the Sleep Anxiety model, thus, the Disease –> Depression –> Sleep pathway again received stronger support.

Lack of confirmation for the Disease –> Sleep –> Depression pathway in the Sleep Anxiety model is not surprising, given weak univariate relationships between SLAM-F and CESD-AR. Despite a similar weak relationship between SLAM-F and Sleep Anxiety, the Disease –> Depression –> Sleep pathway received support, as did reciprocality between Sleep Anxiety and Depression.

Support for the Disease –> Depression –> Sleep pathway in both tests of the model is interesting, since the two sleep factors are not highly correlated and may thus represent distinct constructs. The Sleep Anxiety items are affect-laden (e.g., lying awake anxious, worried or distressed; worrying during the day about how you will sleep at night), whereas the Sleep Disruption items ask about actual sleep disturbance.

Table 2. Two-stage regression analysis of fatigue model using sleep anxiety as the measure of sleep

Equation	Predictor Variable	b_p	Mediator 1	b_{m1}	Mediator 2	b_{m2}	Outcome Variable
1	Disease Activity	0.77*	Sleep Anxiety	5.88**			Depression
2	Disease Activity	0.02	Depression	0.05**			Sleep Anxiety
3	Disease Activity	0.81	Depression	0.39†	Sleep Anxiety	8.31**	Fatigue

Overall R^2 for 3-equation system = 0.42

**p < .01 *p < .05 †p < .15

Discussion

For most people fatigue arising from physical or mental exertion, or acute conditions such as the flu, is of finite duration and often perceived as an adaptive, recuperative process (Piper, 1989a). Generally fatigue is only considered problematic when it becomes chronic, more functionally debilitating, or arises from unclear causes. For women with lupus, fatigue often falls under the latter characterization. In this study the women with lupus reported greater overall fatigue than did a group of women who do not have lupus. Considering various fatigue dimensions, temporal and affective aspects seemed more salient than sensory aspects or severity. Women with lupus were more likely to report chronic, continuous fatigue that had increased recently, instead of describing fatigue as an acute, short-lived experience. They also perceived fatigue in more negative terms, as an unpleasant, abnormal, or destructive experience, rather than as a protective mechanism.

There was only a trend for the women with lupus to report greater fatigue severity, an unexpected finding given other published findings (McCoy et al., 1992; Robb-Nicholson et al., 1989), our pilot interviews (Ouellette et al., 1989) and the lupus group's similarity on the PFS to women with cancer undergoing chemotherapy (Piper, 1992). One explanation may be that the PFS Severity items ask about the degree to which fatigue interferes with life activities, in effect, how well the person is coping with fatigue. Severity may, therefore, not be the best label for this scale. In addition, methodologic considerations probably reduced the possibility of measuring participants' most severe fatigue. The time of day for completing the PFS was not controlled, and the items asked about "fatigue right now" rather than the most severe fatigue of the day. We expect that better methods of administering the PFS would reveal disparate severity ratings between the groups.

The lack of group differences on the sensory aspects of fatigue can be accounted for in two ways. First, sensory aspects of fatigue may not be especially distinctive for women with lupus. Fatigue in many populations or contexts, and arising from various causes may feel very similar. Second, the PFS Sensory items at face value represent varied constructs, including sensation, motivation, emotion, and cognitive functioning. Arguably, all of these may be associated with fatigue, but their utility in distinguishing between populations may be hampered by their being collapsed into a single scale. We did not investigate the factor structure of the PFS items in our sample; rather the four PFS subscales were scored according to Piper's specifications. It will be worthwhile to assess the psychometric properties of the PFS in a lupus sample.

The women with lupus also tended to report more problems with sleep than did comparison group women. Especially noteworthy is their perceived long sleep latencies which may point to sleep initiation problems of clinical significance. Interestingly, they also reported getting more sleep per night. This may reflect a tendency to safeguard sleep and rest time in an effort to control fatigue and other lupus symptoms. Getting more sleep may also reflect a choice available to more of the women with lupus because a greater proportion of them were not working outside the home.

In light of other findings (Krupp et al., 1990; Liang et al., 1984; Robb-Nicholson et al., 1989) it is unclear why there was no group difference in depression in this study. One possible explanation is that the women with lupus may have referred acquaintances for the comparison group who shared not only their demographic characteristics, but also their affective or psychosocial characteristics.

The results of this study lend preliminary support to the following model of fatigue: Precipitated or exacerbated by disease activity, depression and sleep problems can act as mediators or mechanisms that produce or worsen fatigue. Sleep problems, including both sleep disruption and anxiety about one's sleep, are the most proximal link to fatigue in this process.

Nevertheless, the affective component in this model, represented both by the depression and sleep anxiety measures, should not be minimized. The results suggest that this affective component can become linked to sleep disruption in a kind of cyclic process. Depressive symptoms, such as negative ruminations and feelings of low self-worth, can be self-perpetuating. So, too can sleep disturbance and worrying about sleep. After the precipitating circumstances are past, insomnia symptoms can continue because they have become conditioned or associated with bedtime activities, lying in bed, or worrying about getting to sleep (Hauri & Fisher, 1986).

The self-perpetuation of sleep disturbance and depression may be especially salient for people with a chronic "precipitator" such as lupus. In published studies and our own interviews, people with lupus express a great deal of concern about getting plenty of rest and sleep. It may be one of the few ways they feel they can control disease flares. Concern with rest and sleep may also be a way of diffusing some of the depression or other distress they feel because of the challenges lupus brings to their lives. When this concern takes on an anxious quality, it may exacerbate both sleep disruption and psychological distress.

The fatigue model proposed here is preliminary for two reasons. First, the model explained only 48% of the variance in fatigue. Second, methodologic limitations in this study prevented us from testing all possible alternative forms of the model.

The addition of certain explanatory variables would likely improve the model's power and alter its form. For example the SLAM, though a standardized measure of disease activity, is limited. Other aspects of lupus activity or manifestations, such as immunologic components (e.g., cytokines) may need to be included. Also absent from this study are social and environmental context variables, such as stress, social support, and financial resources. Continuing with our program of research, we plan to include such variables to determine what types of effects (e.g., direct, mediational, buffering, etc.) they exert on lupus fatigue. Considering the potential components remaining to be tested in the model, it is encouraging that these results accounted for almost half the variance in fatigue.

Using a longitudinal research design would increase confidence in the fatigue model's form. For instance, perhaps the Disease –> Sleep –> Depression pathway was not supported because fatigue exerts a causal effect on depression (reversing the arrow between depression and fatigue), or perhaps there is another reciprocal relationship between depression and fatigue. Nevertheless, the variables in this study were measured in a way that lends credence to the causal sequence supported by the statistical analyses. Disease activity was assessed for the previous month, sleep and depression for the previous week, and fatigue right now.

The measures of sleep, depression and fatigue were all based on self-report scales. While future work could benefit by including objective measurement techniques, the self-report approach offers both empirical merit and clinical relevance. Self-reported sleep parameters are often well correlated with laboratory measures (Frankel et al., 1976; Hoch et al., 1987; Spielman, 1990; Spielman et al., 1987). The depression measure used here has well-established validity. In a clinical context, patients' subjective symptom experiences influence clinical outcomes such as functional status and quality of life. Describing "fatigue" to a health care provider may be based on a variety of phenomena: physical sensation, motivation, cognitive functioning, affective state, and correspondence to other symptoms. Care providers often identify fatigue through patient self-reports. It is relevant, therefore, to investigate subjectively appraised processes that, either independently or in concert with disease activity, produce the phenomenon subjectively experienced as "fatigue".

In conclusion, while this model is in the process of further development, these early results provide confidence in one conclusion. The mediational effects found for sleep problems and depression rule out the idea that disease activity, as measured by the SLAM, had a direct effect on fatigue in this study group. Instead, disease manifestations had a more proximal effect on depression, sleep disruption and/or sleep anxiety, which then acted as more proximal causes of fatigue. These findings suggest that, in addition to disease-management treatment strategies, existing interventions for sleep pathologies and depressive symptoms should be tested for their efficacy in alleviating lupus fatigue.

Notes

1. The study "Stress and Stress-resistance in Systemic Lupus Erythematosus" (PI: Suzanne C. Ouellette, PhD) was a six-month prospective study of the effects of stress and stress resistance resources on lupus disease flare and psychological distress. The Lupus Stress Study was funded by and conducted in association with the Cornell Arthritis and Musculoskeletal Diseases Center (PI: Charles L. Christian, MD; NIH # P60 AR38520), an NIH supported interdisciplinary research center.

2. The term "marginally significant" is used commonly to refer to statistical results with a p-value near the standard criterion of $p = .05$. We use the term for results within $.051 \leq p \leq .15$. The criterion p-value for some statistical tests, including linear regression-based procedures such as used in this study, varies by sample size. The potential importance of a result, therefore, should be appraised based on the actual strength or level of the statistic, along with the p-value. In this paper several "marginally significant" results are reported because of our appraisal of their worth for guiding future research or their potential clinical significance.

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Chapter 3

Daily Patterns in Fatigue, Sleep and Mood among Women with Lupus and an Acquaintance Referral Comparison Group

Fatigue has become recognized as one of the most prevalent, chronic, troublesome symptoms associated with the rheumatic diseases. Because its etiology remains so uncertain, fatigue is also a difficult, frustrating symptom for health care providers and patients to manage. Researchers recently have been devoting more attention to rheumatic disease fatigue, but the emphasis is primarily on measuring the amount or level of fatigue and its relationship with possible etiological factors. One crucial step toward determining the etiology of a symptom like fatigue is to describe the phenomenon itself. Better description of fatigue phenomenology and time course will serve researchers and health care providers in two ways. First, knowing more about the phenomenological experience of fatigue will help determine its functional impact. The level of fatigue may not be the only dimension explaining why fatigue is debilitating. The lived experience of fatigue involves not only the perceived amount of fatigue, but also sensations, attributions about its causes, emotional responses to fatigue, the timing of fatigue in the context of other life activities, and the perceived consequences of fatigue in one's life. The ways these dimensions differ in rheumatic disease compared to the general population should help care providers respond more specifically in helping patients manage fatigue. Second, both the phenomenology and timing of fatigue may point to possible etiological factors.

The purpose of this paper is to describe fatigue and two factors, sleep patterns and mood, thought to contribute to fatigue among women with systemic lupus erythematosus (lupus) compared to a demographically similar group of women who do not have lupus.

The daily time course and phenomenology of fatigue are described, as well as daily patterns in self-reported sleep parameters and positive affect, a mood dimension associated with depression and fatigue-like states.

While in medical terms fatigue is certainly not the most serious lupus manifestation, from a more biopsychosocial perspective it can be one of the most disruptive. Among people with lupus fatigue prevalence ranges as high as 80-100% (Schur, 1993). More importantly, people with lupus describe fatigue and perceive its impact as debilitating. A great majority of people with lupus (75%) describe fatigue in terms of often "not having enough energy to do what they want" (Robb-Nicholson et al., 1989). Among rheumatic disease groups, people with lupus rank second only to those with fibromyalgia in describing fatigue as one of the worst or most disabling problems associated with their disease (Krupp, LaRocca, Muir, & Steinberg, 1990; Liang et al., 1984; McCoy, Callahan, & Pincus, 1992). Knippen (Knippen, 1988) reports that women with lupus (n=70) describe fatigue as interfering with a variety of activities and life domains: job (27.1%), social activities (22.9%), sleep/rest (21.4%), housework (18.6%), family relationships (15.7%), irritability/cloudy thinking (10%), and depression (8.6%). Of this group 11.4% reported no impact of fatigue. In these descriptive reports people with lupus seem to be saying that fatigue interferes with their daily lives to the point of eroding functional capacity and vitality.

Efforts to define and treat fatigue associated with lupus have been difficult. Based on both patient reports and physician rated disease activity measures, fatigue is usually much worse with increased lupus disease activity (Knippen, 1988; Wysenbeek, Leibovici, Weinberger, & Guedj, 1993). This association is very broad, however, as fatigue is correlated with a variety of lupus signs and symptoms (Wysenbeek et al., 1993). Of the medical strategies for lupus, high dose glucocorticoids and antimalarials are among the few which are effective for fatigue, but only some patients respond to these (Hahn, 1997). Other fatigue management strategies are also limited. People with lupus (70%) often use sleep or rest to manage fatigue (Robb-Nicholson et al., 1989), but many (91%) have experienced fatigue that was not relieved by sleep (Knippen, 1988). Conversely, in one study aerobic exercise was effective in reducing fatigue without exacerbating disease symptoms (Robb-Nicholson et al., 1989). Collectively, these findings argue that fatigue is best characterized as a nonspecific lupus manifestation (Lahita, 1997; Wallace, 1997), yet this definition leaves health care providers with little guidance about how to help patients effectively reduce fatigue.

Fatigue researchers in other disciplines have advocated defining and measuring fatigue as a multidimensional construct (Piper et al., 1989). Some have speculated that it may be most beneficial to consider fatigue as a variety of phenomena manifested differently across situations and populations, rather than seeking a unitary, multidisciplinary definition (Muscio; Bartley; and others cited in Piper, 1986; Piper, 1989). Because lupus fatigue is poorly defined, has uncertain etiology and occurs in a variety of conditions, a broader, multidimensional approach would be especially helpful in understanding it. Two important areas for further study are the phenomenology and time course of lupus fatigue. Studying fatigue phenomenology through a variety of dimensions would help identify areas most problematic to people with lupus versus fatigue dimensions more similar to the normal ebb and flow of fatigue experienced in the general population.

Such richer description will help identify the fatigue dimensions toward which interventions might most effectively be directed.

One important dimension of fatigue is its time course. Piper includes a temporal component in her multidimensional fatigue scale (Piper et al., 1989) which asks about whether fatigue is chronic, continuous versus intermittent, and recent change in fatigue. Belza retains this temporal component in her shorter, revised form of Piper's scale (Belza, 1990); it assesses the past week's fatigue frequency with a single item. While these measures help describe fatigue chronicity in general terms, they do not give a clear picture of the course of fatigue over time. In a prospective study of fatigue, Belza compared people with rheumatoid arthritis (RA) to an age and sex matched control group of people without RA (Belza, 1995). Overall, the RA group reported higher scores on all the fatigue dimensions measured: degree, severity, timing, functional impact, and distress caused by fatigue. When compared on a summary fatigue score across all these dimensions at three intervals of six to eight weeks, the RA group did report higher overall fatigue, but their fatigue did not vary significantly over time.

The descriptive reports from people with lupus suggest that they feel fatigue's impact on a day-to-day basis, but these studies shed little light on the time frames or fluctuation patterns in which fatigue most often occurs. In the general population fatigue fluctuates in a diurnal pattern (Monk, Fookson, Moline, & Pollak, 1985). Most people experience this as part of a normal exertion–rest–recuperation cycle in the course of everyday life (Piper, 1989). At the same time, the prevalence of more extreme, problematic or overly frequent fatigue is also fairly high, ranging from 14-25% (Lewis & Wessely, 1992; cited in Goldenberg, 1995). Women have a 1.5 times higher risk for frequent fatigue than men (Chen, 1986). To evaluate fatigue in the context of lupus, we need better descriptions of fatigue in daily life compared to these patterns and levels of fatigue in the general population.

While fatigue seems to bother people with rheumatic disease on a more chronic, enduring time frame (Belza, 1995), it may occur in acute fluctuating episodes which peak and remit, or it may endure over longer periods at a plateau level. Belza's data on fatigue in RA (Belza, 1995) suggest that we need to observe much shorter intervals to detect salient fatigue fluctuations. There are no published studies describing daily fatigue in lupus, but a few investigators have studied daily and diurnal patterns in fatigue and other symptoms among other rheumatic disease populations. Affleck, et al. (Affleck, Tennen, Urrows, & Higgins, 1991) studied individual daily patterns of RA pain for 75 days. Pain tended to rise and fall frequently, either in discrete outlier spikes on a given day, or in peaks which were anticipated by rising pain for one or more preceding days. For most individuals (87.2% of 33 participants) there was a first-order autocorrelation pattern such that today's pain predicted tomorrow's. For many people (51.5%) the autocorrelated relationship of today's pain to later pain extended from two to nine days, although the one-day lagged effect accounted for most of the longer lagged effects. Although individual differences in daily patterns did emerge, the overall trend of frequent daily fluctuations highlights the importance of a daily level of analysis.

Stone, et al. (Stone, Broderick, Porter, & Kaell, 1997) observed significant diurnal fatigue and pain patterns in RA. Generally fatigue exhibited a j-shaped pattern from morning to night. At 8:00 a.m. fatigue was slightly elevated then dropped to its lowest points from 10:00 a.m. through noon. By 2:00 p.m. fatigue had begun to increase but was not yet as high as in the early morning, and it continued to rise through the rest of the day. The diurnal pattern of pain was different from fatigue. Pain was highest first thing in the morning at 8:00 a.m., then it declined until mid-morning to a plateau which was maintained for the rest of the day. These patterns were derived by averaging across participants, thus they do not reveal whether individual differences in these patterns are common. The authors do report that only 37% (pain) and 34% (fatigue) of thirty participants showed diurnal patterns. The fatigue pattern described is similar to the cycles of "effort" and "weariness" described among a heterogeneous group of healthy participants (mean age = 50.7 yr) (Monk et al., 1985). Diurnal fatigue fluctuations in lupus are suggested by one report that 74% of participants (n=23) felt fatigue is worse between 1:00 p.m. and 5:30 p.m. (Robb-Nicholson et al., 1989). While this single estimate cannot adequately describe a diurnal pattern, it is somewhat discrepant with the diurnal cycle described in RA (Stone et al., 1997). In a retrospective report participants may rate fatigue earlier in the day as more severe than fatigue at the end of the day because it can have more impact on important activities. These findings suggest the worth of exploring both daily and diurnal patterns in lupus fatigue.

If lupus fatigue fluctuates daily, describing this pattern should provide clues about etiological factors contributing to fatigue. Two factors likely related to daily fatigue fluctuations are sleep and mood. Sleep fragmentation, due to sleep disorders such as sleep apnea, or experimentally induced in groups without sleep disorders, causes daytime fatigue and the cognitive sluggishness often associated with fatigue (Bonnet, 1989; Stepanski, Lamphere, Badia, Zorick, & Roth, 1984). Sleep studies of people with fibromyalgia and RA reveal a high prevalence of severely fragmented sleep (Crosby, 1988; Hirsh et al., 1994; Mahowald, Mahowald, Bundlie, & Ytterberg, 1989; Moldofsky, 1993; Moldofsky, Scarisbrick, England, & Smythe, 1975), which has been correlated with fatigue (Anch, Lue, MacLean, & Moldofsky, 1991; Jennum, Drewes, Andreasen, & Nielsen, 1993; Moldofsky, 1993; Moldofsky et al., 1975).

There are no published polysomnography studies of sleep in lupus. In an aerobic exercise study with twenty-three people with lupus, 61% reported rarely awakening refreshed from sleep (Robb-Nicholson et al., 1989). Knippen provided the most detailed subjective description of sleep from her study of seventy women with lupus (Knippen, 1988). Mean sleep latency was 35 mins. Mean total sleep time was 7 hours, consisting on average of 6.5 hours nighttime sleep and a half-hour daytime nap. On awakening 33% felt alert and clear-headed; 21% felt fairly clear-headed, but 43% awakened very drowsy. In terms of overall sleep quality 14% said they had slept badly the night before, while 85% reported sleeping well or very well. In terms of sleep depth, which may be related to sleep fragmentation, 39% said their sleep was light. Generally, 40% of the women were dissatisfied with last night's sleep. On awakening in the morning, 43% felt very drowsy. These data are limited because they are drawn from a single questionnaire asking about the prior night's sleep. They suggest, however, that a substantial proportion of people with lupus perceive sleep to be inadequate along several dimensions.

Daily fatigue is also likely related to daily mood. Depressive symptoms and mood are related to both somatic and cognitive aspects of fatigue. Physical lethargy and cognitive sluggishness, often associated with fatigue, are markers of certain depression syndromes (American Psychiatric Association, 1994). On a more normative level certain mood dimensions and fluctuations in mood are associated with tiredness and other fatigue-related states. Researchers generally define mood as two independent, bipolar dimensions. These dimensions are usually labeled positive and negative affect (PA and NA) (Watson, Clark, & Tellegen, 1988; Watson & Tellegen, 1985); or the analogs energetic and tense arousal to refer to physiological arousal states associated with the dimensions (Thayer, 1989). Positive affect is defined generally as active, pleasurable engagement and alertness, whereas NA is defined generally as subjective distress and dissatisfaction. Low PA is associated with fatigue-related states, including cognitive and physical sluggishness, decreased concentration, and sleepiness. PA is more purely associated with depressed affect, whereas NA contains components of both anxious and depressed states (Thayer, 1989; Watson & Kendall, 1989). Positive affect, thus, is the mood dimension more relevant to fatigue. PA reliably exhibits diurnal fluctuation patterns (Clark, Watson, & Leeka, 1989; Monk et al., 1985; Thayer, 1987), but the peak PA times vary across studies. While this variation occurs partially because of methodological differences among studies, it is also a function of individual differences in peak PA times. Nevertheless, PA tends to peak between noon and mid-afternoon for people on a normal nighttime sleep cycle (Thayer, 1989).

As with fatigue, daily mood patterns among rheumatic disease populations have received little attention. In their daily diary study of RA pain, Affleck, et al. (Affleck, Tennen, Urrows, & Higgins, 1992) also investigated causal relationships among neuroticism, pain, and negative mood. They describe overall trends in mood based on participants' individual time series across 75 days. In general, people with RA tended to experience few days of unusually high negative mood. For 39.2% of participants, negative mood tended to decrease over time, exhibited through a linear trend in the time series; but for 9.5% negative mood tended to increase over time. Similar to this group's findings for daily pain, for 48.6% of participants there was a significant first-order autocorrelation for daily negative mood. Mood today tended to predict the next day's mood.

The mood measure used in the RA pain study (Affleck et al., 1992) assesses depression, anxiety and hostility, i.e. negative affect instead of positive affect, which reflects a common bias in mood research. Further, the research questions in this study reflect a trend in the psychology literature to investigate the causes and outcomes of negative affect (e.g., (Bolger, DeLongis, & Kessler, 1989; Gaskin, Greene, Robinson, & Geisser, 1992; Vassend, 1994; Zautra, Guarnaccia, & Reich, 1989). In contrast, most research relevant to mood in rheumatic disease has been in the area of depression and depressive symptoms (Blalock & DeVellis, 1992; DeVellis, 1993; Katz & Yelin, 1993). Living with a chronic illness is seen as increasing one's risk for periodic depressive states, as well as major depression episodes. In trying to describe lupus fatigue and related mood states more fully, it seems more relevant to focus on PA. Given the closer links among fatigue, depression and PA, rather than NA, and the focus on depressive states in rheumatic disease research, it may be more useful to describe daily PA patterns in comparison to daily fatigue patterns.

In the study reported here daily fatigue, sleep patterns, depressive symptoms and positive affect were assessed with a fourteen-day diary. Among the studies of fatigue, sleep or mood in rheumatic disease, very few include a comparison group. Here, a demographically matched comparison group was included to compare not only the levels but also the day-to-day patterns in fatigue, sleep characteristics and mood among women with lupus. These findings replicate and extend those obtained in a prior cross-sectional study and reported in Chapter 2 (McKinley, Ouellette, & Winkel, 1995).

The phenomenology of fatigue is explored using a weekly multidimensional subjective measure. Based on the cross-sectional findings, I hypothesized that for women with lupus, the sensations defining the fatigue experience would not differ from those reported by their peers. Instead, lupus fatigue is expected to differ along an affective dimension on which women perceive fatigue as a more negative, abnormal, destructive experience rather than as a protective mechanism; and a temporal dimension, reflecting more chronic, continuous fatigue.

The temporal course of fatigue was examined more fully than in the cross-sectional study through daily fatigue ratings twice a day. While women were expected to describe fatigue generally as a chronic problem on the multidimensional fatigue measure, daily fatigue was expected to reveal fluctuating, autocorrelated patterns from day-to-day. In terms of fatigue severity, i.e. the level of fatigue, the cross-sectional results revealed only a marginally significant difference, but this was a surprising finding given other reports in the literature. As explained in Chapter 2 (McKinley et al., 1995) methodology may have masked the group difference in fatigue severity. In this study the women with lupus were expected to rate fatigue higher than their peers during the day but not at bedtime, when diurnal fatigue peaks for everyone.

Several nightly sleep parameters were explored in this study. The lupus group was expected to report poorer quality sleep through longer sleep latencies, more wake time during the night, lowered sleep efficiency and/or lower subjective overall sleep quality. In spite of sleep quality differences, the lupus group was not expected to report lower quantities of sleep. Polysomnography sleep studies in rheumatic disease groups reveal considerable sleep fragmentation but not lower total sleep time (Hirsh et al., 1994; Mahowald et al., 1989; Moldofsky, 1993). In my cross-sectional study there was a trend toward longer sleep times among the women with lupus, but this may reflect the common concern in this group for getting plenty of rest and sleep (Ouellette, Bochnak, & McKinley, 1989; Robb-Nicholson et al., 1989).

Finally, prospective patterns in depressive symptoms and mood were explored using both a standard self-report depression measure and daily positive affect ratings during the day and at bedtime. Positive affect was expected to show a time of day effect in both groups, with higher PA during the day than at bedtime. Positive affect can reflect fatigue-related states; therefore, as hypothesized for daily fatigue, PA was expected to be lower for women with lupus than their peers during the day but not at bedtime. Based on the cross-sectional results, however, the lupus group was not expected to report overall higher depressive symptoms or lower positive affect than women without lupus.

Method

Participants

Daily diary data from thirty-three women with SLE and thirty-seven comparison group women who do not have SLE are reported here. Information provided in a baseline questionnaire was used to screen participants for eligibility criteria and control for sleep-wake cycle confounds. Women in both groups were ineligible to participate if they: were pregnant; had a child under one year of age; worked night shift work; were outside the ages of 20 to 50; had attained less than a high school diploma or the equivalent. Comparison group participants were excluded if they had any diagnosed rheumatic disease. Effort was also made to exclude those taking sedative or psychoactive medications; however, due to the difficulty recruiting participants for this protocol, a few women in both groups were taking either sedatives or antidepressants during the study (Table 1).

Women with a diagnosis of SLE were recruited from a patient registry established through the Cornell Arthritis and Musculoskeletal Diseases Center (AMDC). Four rheumatologists affiliated with the Hospital for Special Surgery in New York whose patients are listed in the registry gave consent for their patients to be recruited. They also agreed to complete lupus disease activity measures for their patients who enrolled in the study. All women in the registry aged 20 to 50 with an SLE diagnosis were sent a letter from their doctor describing the study and informed consent forms. Of the women who enrolled in the study, nine were currently seeing physicians outside HSS as their primary lupus doctor. These nine physicians were contacted and agreed to complete the lupus disease activity measures for their patient.

A total of forty-three women with lupus enrolled in the study, and forty-two completed the baseline questionnaire. Seven of these women did not return a complete daily diary for these reasons: lupus-related illness or surgery (2); had a child under one year of age (1); either could not be reached to begin the diary or began the diary but withdrew (3); completed the diary but the materials were lost in return mail (1). Two women completed the diary but were excluded from data analyses. One woman's diagnosis was unclear; her rheumatologist was using a working diagnosis of RA and amyloidosis, not SLE. The other woman was bedridden due to recent surgery for femoral

Table 1. Number of participants in final sample taking sedative or antidepressant medication

	Sleep Medications				Antidepressants			
Group	Baseline	Diary Day 1	Diary Day 7	Diary Day 14	Baseline	Diary Day 1	Diary Day 7	Diary Day 14
Lupus	6	3	4	3	3	2	3	3
Comparison	2	1	0	1	2	2	2	2

aseptic necrosis, and her responses on many variables across multiple days were outliers relative to the other women's responses.

Upon study enrollment, the women with lupus were asked to refer for study participation five female acquaintances similar to themselves in age, education and ethnicity who do not have lupus. Comparison group participants were recruited from this pool of names; however, it was soon apparent that this pool was not large enough. To increase the comparison group recruitment pool, women without lupus who enrolled were also asked to provide acquaintances' names. Because this personal referral method threatens participants' confidentiality, each woman was assured that her identity would not be revealed to her acquaintances; however, she could certainly choose to inform her acquaintances that she was providing their names for the study. Further to insure confidentiality, the women without lupus were not told that the study's focus was on lupus.

All acquaintances referred to the study were sent letters and informed consent forms. They were asked to participate in a women's health study which addressed the daily experiences of women and the ways these experiences affect how one feels each day, including issues of fatigue, sleep, mood and health symptoms. The letter explained that another woman in the study had referred them. This acquaintance referral method has produced a demographically similar comparison group in a study of chronic facial pain (Marbach, Lennon, & Dohrenwend, 1988) and in the study of stress and lupus (Ouellette Kobasa et al., 1991), through which the cross-sectional fatigue study reported in Chapter 2 was conducted.

A total of forty-nine women without SLE enrolled; forty-four of these completed the baseline questionnaire. Seven women did not return a complete daily diary for these reasons: had a diagnosed rheumatic disease, including RA (1) and arthritis associated with ulcerative colitis (1); began the diary but withdrew from the study (3); currently pregnant (1); completed the diary but the materials were lost in return mail (1).

The acquaintance referral method was very successful in recruiting a comparison group demographically similar to the lupus group. Table 2 lists demographic characteristics of the groups. The groups were similar in age, education and ethnicity, the characteristics women were asked to use in choosing referrals. They were also similar along several social participation variables which might be influenced by living with a chronic illness such as lupus. These include relationship and parenthood status. A smaller proportion of the women with lupus were working outside the home. This sampling difference is almost unavoidable given the increased rate of disability in the lupus population. In this sample seven women with lupus who were not working received disability benefits.

The thirty-three women with lupus who completed the study were experiencing relatively mild disease activity. Rheumatologists for thirty-two women completed the

Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), a measure of current disease activity (Bombardier et al., 1992). Average SLEDAI scores (*M* = 5.56, *SD* = 5.65) were similar to those reported in a recent descriptive study comparing current disease activity and cumulative organ damage due to lupus (*M* = 4.1, *SD* = 5.3) (Hanly, 1996). This group tended to have milder disease activity than the 574 patient profiles reported in the SLEDAI validation study, however (Bombardier et al., 1992). All thirty-two women scored ≤ 20 on the SLEDAI, whereas in the validation study only 80.7% scored within that range, with the remaining 19.3% scoring between 20 and 45. Both the participants and their physicians marked two 100 mm visual analog scales on a scale from 0 to 100. The two ratings assessed current disease activity (from "none" to "most") and overall lupus case severity (from "least severe" to "most severe" case). The women rated current disease activity slightly higher than their physicians (means: participants = 37.53; doctors = 26.28; $t(31) = 2.55$, $p = .02$). Some of this discrepancy may be due to the time lag (generally one month or less) between when the participants and doctors completed these ratings. Participants and their doctors judged the overall severity of their case of lupus similarly (means: participants = 36.03; doctors = 39.69; $t(31) = -0.78$, ns).

Table 2. Participant demographics

	Lupus (n=33)	Comparison (n=37)	Difference
Age	38.27	38.02	$t(68) = .13$
Education (yrs)	16 (B.A.)	16 (B.A.)	$t(68) = -.42$
Race/Ethnicity:			$\chi^2(3) = 4.41$
African American	21.2%	13.5%	
Asian American	6.1%	0.0%	
Latina	3.0%	10.8%	
White	69.7%	75.7%	
Median Income:			
Household	$70,000-79,999	$55,000-65,000	$\chi^2(5) = 3.61$
Self	$30,000-39,999	$30,000-39,999	$\chi^2(5) = 4.99$
Work Status:			$\chi^2(4) = 11.57^*$
Full-time	51.5%	78.4%	
Part-time	21.2%	5.4%	
Student	3.0%	0.0%	
Disabled/Unemployed/ Retired	18.2%	2.7%	
Homemaker	6.1%	13.5%	
Relationship status:			$\chi^2(4) = 3.82$
Married/Living with partner	63.6%	56.7%	
Relationship/Dating	6.0%	13.5%	
Separated/Divorced	15.2%	8.1%	
Single	15.2%	21.6%	
Parenting	45.5%	37.8%	$\chi^2(5) = 4.47$

* $p < 0.05$

Measures

Measures of fatigue, sleep quantity and quality, and depressive symptoms and mood were collected prospectively through a daily diary format. Baseline measures of these constructs were collected and used as covariates in the analyses reported below.

Fatigue

Multidimensional fatigue. As in the cross-sectional study, the Piper Fatigue Scale (Piper et al., 1989) was used to assess various dimensions of the fatigue experience. The PFS was completed at the beginning (night 1), middle (night 7) and end (night 14) of the two-week diary to examine the course of these dimensions over time. In the cross-sectional study, several limitations in the PFS arose and are discussed in Chapter 2. In addition there was a nonrandom, high rate of missing data on certain items. When asked only about fatigue "now" participants experiencing no current fatigue left many items blank because they were irrelevant.

In this diary study attempts were made to control these methodological and psychometric sources of confounding. Participants were asked to complete the PFS within one hour of bedtime to control for time of day effects. Participants were asked to rate both how they felt right now and during the past 24 hours for each subscale. The "24 hours" version increased the chance that women had some experience of fatigue on which they could base subsequent items' ratings. The rate of missing items was lower using this approach. To capture the most severe fatigue of the day, each woman's final score was calculated as the higher of the "right now" and "24 hours" scores on each subscale.

Finally, the psychometric properties of the PFS were examined with factor analyses. Because of the small sample size relative to the 39 items on the PFS, an overall factor analysis including all items from the PFS was not feasible, nor was this approach most relevant. The primary goal was to explore the structure of Piper's severity and sensory scales because they did not reveal group differences in the first study. A secondary goal was to confirm that the factor structure of the remaining subscales agreed in this sample with Piper's item groupings. Using only the lupus group's data, each of Piper's original four subscales was subjected to exploratory factor analysis with oblique rotation. The subscales' structures at nights 1, 7 and 14 were examined in separate analyses to explore factor structure variations over time. After looking across the results over time, however, standard item groupings were used to score the new subscales the same way at each time point.

Based on these factor analyses, I redefined the PFS as representing nine fatigue dimensions, rather than four. The temporal course or chronicity of fatigue, and affective attributions about fatigue remained distinct factors defined by the same items as in Piper's original scale. Piper's sensory subscale was redefined as five factors that I labeled as tiredness, cognitive changes, sleepiness, anxiety, and low motivation. Piper's fatigue severity dimension was split into two factors: severity (or level) of fatigue; and fatigue consequences, i.e., the impact of fatigue on activities of daily living and social interactions. The scale items and Cronbach's internal reliability alpha coefficients for these new scales at all three time points are listed in Appendix C2.

Daily fatigue. To assess prospective patterns in daily fatigue, participants twice daily rated a single 100 mm visual analog scale (VAS). The question, "To what degree are you experiencing fatigue right now?" was rated from 0 (No fatigue) to 100 (A great deal of fatigue). This item is drawn from the Piper Fatigue temporal subscale and is intended as an overall index of current fatigue.

Baseline fatigue. The PFS was not included in the baseline questionnaire, so no baseline covariates were used in analyses involving the PFS subscales. A general measure of the past month's fatigue severity, The Fatigue Severity Scale (FSS) (Krupp, LaRocca, Muir-Nash, & Steinberg, 1989), was used as a baseline covariate for the daily diary fatigue ratings. The FSS contains nine items describing functional effects of fatigue (e.g., fatigue interferes with physical functioning, fatigue interferes with certain duties and responsibilities). Items are rated on a seven-point scale from "strongly agree" to "strongly disagree". Internal reliability for the FSS was good ($\alpha = 0.91$). The FSS was developed for chronic illness populations. Krupp, et al. (Krupp et al., 1989) found the FSS indicated more severe fatigue in a lupus group than in a multiple sclerosis group, both of whom had higher scores than a healthy comparison group.

Sleep Quantity and Quality

Daily sleep log. A standard sleep log format was used to assess daily sleep patterns. Each morning, participants described last night's sleep using several variables. Standard sleep parameters for each night were derived from these reports.

Nightly time spent in bed was calculated two ways. The more traditional measure in sleep research is to calculate time spent in bed while trying to sleep (TIBSLP). In this study TIBSLP was calculated as the difference between the time of day participants began trying to fall asleep at night (TRYSLP) and the time of day they woke up for the last time and did not return to sleep (WAKEUP). A second measure of time in bed was calculated to assess bed rest behavior. Women with lupus report using rest as a fatigue management strategy (Robb-Nicholson et al., 1989). Although participants did not report daytime rest periods, they did record time spent in bed before and after nighttime sleep. The measure of total time in bed (TIBTOT) is the total time between getting into bed at night (INBED) and getting up out of bed after the final morning wake-up (OUTBED). Women in both groups routinely spent some time in bed before trying to sleep (INBED–TRYSLP interim); likewise, they often remained in bed after awakening in the morning (WAKEUP–OUTBED interim). Total time in bed includes those rest times.

Each night participants estimated the time it took to fall asleep, or sleep latency (SLAT). They also reported number of awakenings and estimated the total time awake during the night after sleep onset (WASO). Total nightly sleep time (TST) was calculated as the total time trying to sleep (TIBSLP) minus SLAT and WASO. Sleep efficiency (SE%), a common summary measure of sleep quality, is the percentage of time in bed one is actually sleeping (TST / TIB x 100). In clinical evaluations, sleep efficiencies below 80% generally indicate a significant sleep disorder. Using both measures of TIB, SE% was calculated two ways, as sleep efficiency based on total time in bed including rest time (SE_TIB%); and sleep efficiency based on time in bed trying to sleep (SE_SLP%). Finally, each morning participants rated their past night's sleep quality (SQUAL) on a scale from 0 (very good, restful or refreshing) to 10 (poor, restless or unrefreshing).

Baseline sleep. Baseline estimates of average sleep latency, total sleep time, time in bed, sleep efficiency, and subjective sleep quality during the past month were used as covariates for the analogous daily diary sleep measures. These baseline measures were obtained from component scores on the Pittsburgh Sleep Quality Index (PSQI) (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). The PSQI contains no measure of wake time after sleep onset (WASO) to use as a covariate for the daily diary WASO measure. The PSQI's seven component scores and global score are valid in distinguishing a healthy control group from these clinical groups: those with disorders of initiating and maintaining sleep, the insomnias (DIMS); those with disorders of excessive somnolence, narcolepsy and related disorders (DOES); and clinically depressed patients.

Depressive Symptoms and Mood.

Depressive symptoms. Depressive symptoms were assessed at baseline as a covariate measure and weekly throughout the daily diary. The Center for Epidemiological Studies Depression scale (CESD) asks about affective and somatic depressive symptoms. Participants rate the degree each item has described their feelings in the past week on a four-point scale from "rarely (less than 1 day)" to "most of the time (5-7 days)". Possible scores range from 0 to 60 (Appendix E1). The CESD has very good psychometric properties in the general population, reflects current symptomology and is sensitive to change after life events expected to affect depressive symptomology (Radloff, 1977). Four of the twenty scale items have been shown to inflate the incidence and severity of depression in people with rheumatoid arthritis (Blalock, DeVellis, Brown, & Wallston, 1989). These items are face valid indicators of sleep disruption and fatigue. In this study, therefore, revised CESD scores without the four biased items were used.

Daily mood. Twice daily, participants rated their mood with the Positive and Negative Affect Schedule (PANAS) (Watson et al., 1988). The PANAS consists of two 10-item mood adjective lists (Appendix E2). Participants rate whether each adjective has described their feelings within a specified time period on a five-point scale from "very slightly or not at all" to "extremely". Possible scores range from 10 to 50 on each scale.

These scales assess two primary mood dimensions, positive affect (PA) and negative affect (NA) (Watson & Tellegen, 1985). Because the two dimensions show consistently low intercorrelation in factor analytic studies (r = -.12 to -.23) and from validation studies in both normal and clinical populations, PA and NA are conceptualized as independent, bipolar factors (Kendall & Watson, 1989). NA contains components of both anxious (e.g., afraid, nervous, worried) and depressed (e.g., sad, lonely, blue) states. Low PA, conversely, more purely reflects depressed affect. Because the interest for this paper was in depressed affect, only the PA scores were used in analyses. Various investigators have found low PA associated with fatigue-related states including cognitive and physical sluggishness, decreased concentration, and sleepiness (Thayer, 1989; Watson & Kendall, 1989).

Procedure

Participants in the study completed a baseline questionnaire, followed by a daily structured diary for fourteen days. Women who returned a signed consent form were mailed the baseline questionnaire. This packet contained questions to screen for study eligibility, the covariate measures described above, and demographic information. After returning the baseline survey, women who met eligibility criteria were contacted by phone to schedule a convenient date to begin the daily diary. The diary was scheduled to begin as soon as possible after each woman had an appointment with her rheumatologist. In most cases the diary began within a month after a physician visit. For that targeted appointment date, the rheumatologist was asked to complete an ARA lupus diagnostic criteria checklist (Tan et al., 1982) to verify SLE diagnosis and the SLEDAI disease activity measure. For the women without lupus, the diary was scheduled at any convenient time. For both groups the diary was preferably scheduled when the women would not be traveling away from home.

Daily diary protocols require dedication and consistency from participants. In order to engage these women in the process of keeping the diaries, a researcher was paired with each woman upon enrollment, maintained contact with her and kept track of her progress through the protocol. Researchers involved in the study were the investigator and three advanced undergraduate psychology students working as research assistants. On or before each woman's diary start date, a researcher met in person with her. This meeting was meant to establish rapport and familiarize her with the protocol. By explaining specifically what type of information the diary questions addressed, we encouraged the women to be trained observers actively involved in this process. This personalized interaction was also intended to minimize missing data. For example, the sleep log section asked for very specific variables regarding sleep schedules. Women were asked the time each night when they physically got into bed and the time they began trying to fall asleep. We asked them to distinguish between two activities they might not otherwise have considered distinct. We clarified that the times they recorded for these variables might sometimes be the same (e.g., you turn off the lights and try to sleep immediately upon getting into bed) and other times differ (e.g., you get into bed and read for 30 min before turning out the light). The women were encouraged to ask questions both at this meeting and throughout the diary, and were provided with phone numbers to contact both the researcher working with them and the investigator.

Everyone began the diary on a Thursday morning with a practice run-through of the daily diary protocol. Data from this practice day were not analyzed. Officially the diary began Thursday night (night 1). On each Thursday night (nights 1, 7, and 14) participants completed a written questionnaire containing the lupus symptoms severity measure. From Friday morning (day 1) through the second Thursday (day 14) participants completed a fourteen-day telephone call-in procedure. This procedure is a modified version of one used successfully at the City College of New York Sleep Disorders Center (Spielman, Saskin, & Thorpy, 1987). Soon after getting out of bed each morning, participants filled in information in a booklet, with each day's report designed as a script in first-person voice. Each morning's script included last night's sleep log and information not analyzed for this paper, including: past 24 hours' lupus and non-lupus health symptoms; caffeine and alcohol intake; and exercise (example diary page in Appendix D). Participants then called a voice-mail answering system and read the scripted diary report. The women were also encouraged to leave any procedural or other questions on the answering machine with their diary report. Each woman's researcher retrieved daily her call-in data and placed a reminder call to her that same day if she had forgotten to leave a report. The researchers also called participants once or twice during the diary to maintain rapport and answer questions as needed.

The daily fatigue VAS and PANAS were completed in written questionnaires. Based on baseline data, the typical midpoint of each woman's waking day was calculated. The women were asked to complete the fatigue and mood ratings at that midpoint time, usually in mid-afternoon, and again just before getting into bed. These times assessed mood for the first and second halves of a woman's day and fatigue, as the outcome, at the midpoint and end of her day.

Participants received $5 along with the baseline questionnaire and another $35 after completing the two-week diary. The money was offered to participants to thank them for their help and to cover any telephone charges they may have incurred to complete the daily call-in reports.

Results

Prospective patterns of fatigue, sleep, depressive symptoms, and mood in the lupus and non-lupus groups were compared using a repeated measures analysis of variance (RANOVA) approach. Using this approach group differences over time could be analyzed without collapsing the daily data into summary means.

Data analysis. Procedure 5V in the BMDP statistical software provides the means to test RANOVA models and to determine the presence of cyclic, i.e. autoregressive properties in data sets with too few observations for time series models (Dixon, 1992). This program performs repeated measures analysis of variance (RANOVA) using a maximum likelihood estimation algorithm. Unlike traditional RANOVA programs, the 5V program provides a summary table of the main and interaction effects in a model using Wald tests of significance, which are distributed as chi-square statistics (Dixon & Merdian, 1992). Post hoc tests allowing comparisons of means in different conditions are not provided with BMDP 5V. An alternative, however, is that 5V breaks down each effect tested in a complex model into single degree of freedom regression parameters, i.e. unstandardized beta weights and corresponding z-score significance tests. If a main effect has three levels, a significance test is provided for the first two levels (k-1) entered into the design. The significance tests are based on each level's comparison to the overall mean for the effect, thus they allow a kind of post hoc exploration of the results. They do not allow testing contrasts among specific means in the model, however.

A special feature of BMDP 5V allows one to examine cyclic trends in the relationships between sequential data points. Specifically, the 5V procedure is designed to accommodate different types of structures in the covariance matrix. Generally, RANOVA analyses are based on the assumption that the covariance matrix exhibits compound symmetry. Using a log maximum likelihood estimator, Procedure 5V allows one to test alternative covariance matrix structures: compound symmetry, autoregressive, banded autoregressive, and unstructured. Both the log maximum likelihood estimator (ML) and a fit statistic called Aikaike's information criterion (AIC) can be used to assess how well each type of matrix fits the observed data. If there were a prospective pattern or cycle in daily fatigue, for example, it would be expected to appear through one of the autoregressive matrix structures. Fatigue in the afternoon would be expected to predict, i.e. be regressed upon by fatigue at bedtime and possibly fatigue the next afternoon and later. In Procedure 5V, a first-order autoregressive structure would indicate a one-point lagged relationship in daily fatigue, but the relationship does not last beyond the next data point. A banded autoregressive structure would indicate that the regressive relationship continues for at least two data points (Dixon & Merdian, 1992).

In both groups of women there were a substantial number of outlier scores among the daily variables, producing skewed distributions. Standard transformations (e.g., log and square root) were performed in attempts to normalize the distributions. Because the daily variables were used in repeated measures analyses, however, the same transformation had to be performed on all fourteen days of a given variable. Typically a given transformation normalized some days of data but worsened the skew in others. As an alternative, univariate outlier scores in each group's distribution were recoded to be one unit beyond the most extreme non-outlier score. This procedure reduces the outliers' impact on central tendency and variability but preserves their ordinal position in the distribution (Tabachnick & Fidell, 1996). Outliers were identified with the SPSS Examine procedure (SPSS, 1994) as values more than 1.5 interquartile range units beyond either the first or third quartile of the distribution.

Design. The daily variables were examined in a 2 (group) by 14 (days) model. For daily fatigue and positive affect, which were measured at two times of day, a time of day within-subjects factor added to the analyses to create a 2 (group) by 2 (times of day) by 14 (days) model. The PFS subscales and the CESD, which were measured at nights 1, 7 and 14 of the diary, were analyzed in a 2 (group) by 3 (night) design. To address the stated hypotheses, the main effect of the between subjects grouping factor, the main effect of the within-subjects time of day factor, and the group by time of day interaction effect were tested. To determine whether fatigue, sleep and mood occurred in cyclic patterns, or whether they occurred somewhat randomly day-to-day, the data were tested against the different covariance matrix structures, as described above. Finally, a baseline measure of the outcome variable, when available, was entered into the analysis as a constant covariate to control for effects of the general level of the outcome on its daily fluctuations. Some variables showed a marked weekend—weekday difference. To explore this day of week pattern further, a one-way analysis was performed for the lupus group only. The single degree of freedom significance tests provided by BMDP 5V for the day effects were examined. The program provides significance tests for only the first thirteen of the fourteen days (k-1). These tests and their results are discussed in the results section by outcome variable.

The results of these between groups analyses are summarized in Table 3. In the repeated measures analyses, the outlier-corrected distributions generally produced the same results as the original, raw score distributions. Table 3 notes analyses in which the results differed between the two distributions.

Table 3. Between groups comparisons of fatigue, sleep, mood and symptoms[a] (notes appear on final page of table)

Variable	Lupus mean (std dev)	Comparison mean (std dev)	Effect	beta[b]	Wald χ^2	p[c]	Covariance Matrix Structure
Fatigue:							
Daily Fatigue (midday & bedtime)	Day: 40.60 (22.55) Night: 52.58 (25.52)	Day: 34.92 (16.25) Night: 55.62 (21.95)	Group Time of Day Group by Time of day	-2.00 -8.17 2.17	0.86 76.76 5.45	ns < 0.0001 0.02	Banded autoregressive
PFS Temporal	41.78 (19.78)	37.62 (15.04)	Group	2.08	1.09	ns	First order autoregressive
PFS Affective	58.38 (20.80)	45.06 (23.26)	Group	6.66	6.56	0.01	First order autoregressive
PFS Severity	42.48 (21.94)	34.20 (19.96)	Group	4.14	2.79	0.10	First order autoregressive
PFS Tired	67.57 (17.11)	63.17 (17.38)	Group	2.20	1.21	ns	First order autoregressive
PFS Sleepy	60.46 (19.03)	62.71 (20.12)	Group	-1.12	0.24	ns	First order autoregressive
PFS Cognitive	34.46 (20.82)	36.71 (19.91)	Group	-1.12	0.23	ns	First order autoregressive
PFS Anxiety	32.92 (17.89)	31.35 (24.17)	Group	0.78	0.09	ns	First order autoregressive
PFS Motivation	50.12 (17.36)	49.80 (22.01)	Group	0.16	0.01	ns	First order autoregressive
PFS Fatigue consequences	32.97 (20.78)	21.56 (19.66)	Group	5.71	5.61	0.02	First order autoregressive
PFS Overall	46.79 (14.22)	42.46 (15.87)	Group	2.38	1.81	ns	First order autoregressive

Variable	Lupus mean (std dev)	Comparison mean (std dev)	Effect	beta[b]	Wald χ^2	p[c]	Covariance Matrix Structure
Sleep:							
Total sleep time	415.30 (60.02)	413.46 (38.32)	Group[d]	9.36	3.69	0.055	Banded autoregressive
Time in bed trying to sleep	465.05 (53.16)	444.34 (38.89)	Group	4.84	1.16	ns	Banded autoregressive
Time in bed total	521.58 (62.91)	490.61 (42.21)	Group[e]	7.98	3.08	0.08	Banded autoregressive
Sleep latency	17.94 (12.20)	10.51 (6.36)	Group[d]	2.67	6.97	0.008	Unstructured
Wake time after sleep onset	22.23 (17.79)	10.19 (6.30)	Group	6.02	15.33	0.0001	Unstructured
Sleep efficiency (based on time trying to sleep)	90.36% (6.33)	94.32% (3.13)	Group[f]	-1.28	4.85	0.03	Unstructured
Sleep efficiency (based on total time in bed)	80.53% (9.15)	85.15% (5.42)	Group	-0.69	0.64	ns	Unstructured
Self-rated sleep quality	3.99 (2.09)	2.78 (1.77)	Group	0.49	4.38	0.04	Banded autoregressive

Variable	Lupus mean (std dev)	Comparison mean (std dev)	Effect	beta[b]	Wald χ^2	p[c]	Covariance Matrix Structure
Mood:							
Positive Affect	Day: 26.96 (7.44)	Day: 28.79 (7.60)	Group	-0.79	0.80	ns	Banded autoregressive
			Time of day	2.07	68.98	< 0.0001	
	Night: 23.08 (7.24)	Night: 24.39 (8.71)	Group by Time of day	-0.13	0.26	ns	
Depression (CESD)	10.54 (8.50)	11.66 (11.47)	Group	-1.48	2.63	0.11	Unstructured

[a] All analyses were conducted on two data sets: original raw score distributions, and distributions in which outlier scores were corrected by winsorizing. The outlier-corrected results are reported here. The few results that were discrepant between the data sets are noted.

[b] Unstandardized regression parameter estimates. These indicate the predicted amount of change in the outcome variable for each unit change in the predictor variable.

[c] Marginally significant results ($p < 0.15$) are reported to indicate trends worth noting.

[d] TST, SLAT: This effect was marginally significant ($p < .10$) when tested with raw data.

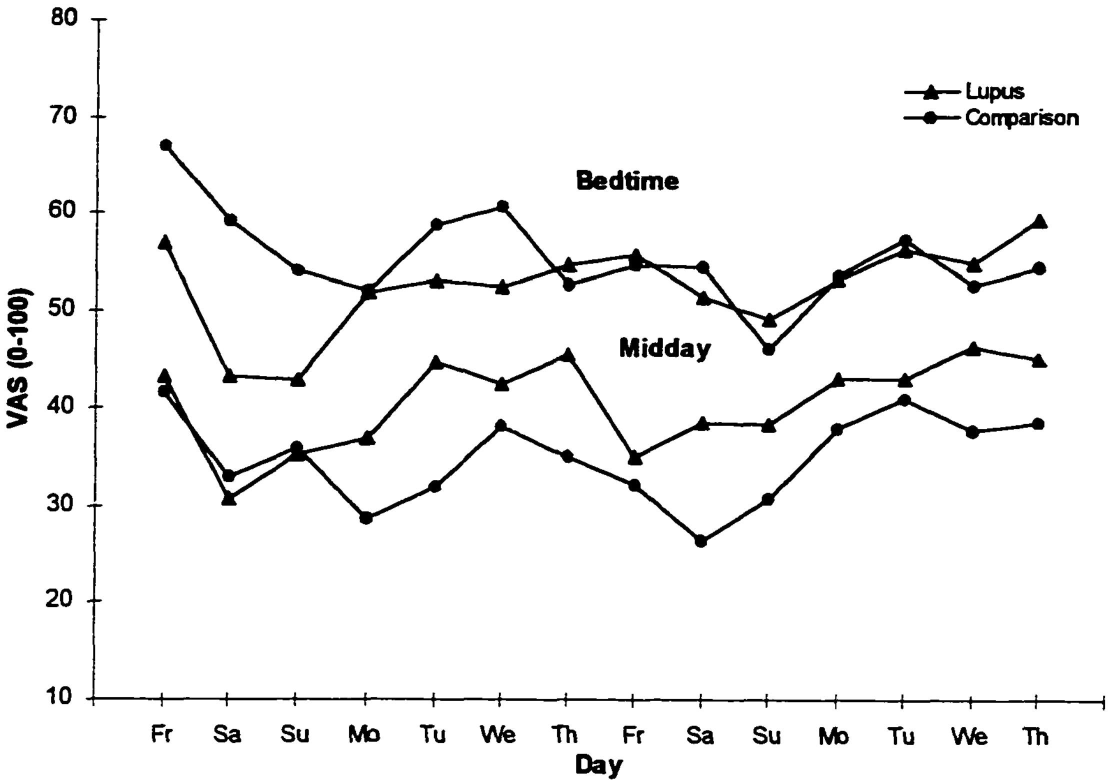
[e] TIBTOT: This effect was significant ($p = 0.04$) using raw data.

[f] SE_SLP: This effect was marginally significant ($p < .15$) when tested with raw data.

Fatigue dimensions. Each PFS subscale was examined as a dependent variable in a series of analyses to assess group differences in the various fatigue dimensions. As in the cross-sectional study, women with lupus reported more negative attributions about fatigue than their peers on the PFS affective subscale. There was a marginally significant trend for higher fatigue severity among the lupus group. Women with lupus also reported more negative consequences of fatigue in terms of limiting various activities of daily living and social activities. In keeping with the cross sectional findings, the phenomenology of fatigue, in terms of tiredness, cognitive changes, sleepiness, anxiety, and low motivation, did not differ between the groups. Contrary to earlier findings, however, women with lupus reported neither more chronic, continuous fatigue on the temporal subscale nor more overall fatigue on the global PFS scores. All the PFS subscales exhibited a prospective trend through a first-order autoregressive covariance matrix. This pattern indicates that fatigue ratings one week predicted the next week's ratings.

Daily fatigue. Group differences in midday and bedtime daily fatigue were compared, using the FSS scores as a constant covariate to control for baseline fatigue. As expected, the experience of daily fatigue is not a stable phenomenon. There was considerable variability over time (Figure 1). There was a time of day main effect in which both groups reported higher fatigue at bedtime than during the day, not surprisingly. There was not a significant group main effect; however, as hypothesized, there was a group by time of day interaction effect. The lupus group generally reported higher fatigue than their peers at the midpoint of their waking days, but not at bedtime. Because midday fatigue was already elevated, on average women with lupus reported only a twelve-point increase

Figure 1. Midday and bedtime fatigue



between midday and bedtime fatigue. The women without lupus reported an average twenty-point increase from midday to bedtime.

The fatigue data were best modeled by a banded autoregressive covariance matrix. This indicates, for example, that fatigue this afternoon predicts fatigue tonight, tomorrow afternoon, and possibly later fatigue. The fatigue pattern across days was examined further in the lupus group in a one-way analysis with fatigue for fourteen days as the outcome. Significant main effects of day and time of day emerged. The single degree of freedom tests provided by BMDP 5V for the day main effect (collapsed across time of day) were examined to determine if fatigue tended to change on certain days of the week. On the first weekend, Saturday and Sunday, fatigue was significantly lower in the lupus group than their overall mean fatigue rating. This pattern was not repeated on the second weekend. These univariate significance test results are presented in Table 4.

Daily time in bed. Group differences in total time in bed and time in bed trying to sleep were assessed in separate repeated measures analyses. Participants' baseline estimate of average time in bed from the PSQI was entered as a constant covariate. Regarding TIBSLP, there was not a main effect for an overall group difference. When the pre- and post-sleep bed rest periods are added to obtain total time in bed, a marginally significant group difference emerges. Group mean differences in TIBTOT ranged from 4.39 to 52.26 minutes across the two weeks.

The banded autoregressive covariance structure in both the TIBSLP and TIBTOT indicates that tonight's time in bed predicts the time spent in bed for at least the following two nights. Here, this structure reflects a striking reduction in weeknight (Sunday through

Table 4. Day effects in the lupus group for selected variables.

Day [a]	Midday Fatigue [b]	Time in Bed total	Total Sleep Time	Sleep Efficiency [c]
Thurs	—	-17.31	-28.33 *	-2.81 †
Fri	2.73	39.24 **	28.98 *	-0.77
Sat	-9.84 **	63.90 **	40.58 **	0.88
Sun	-5.38 †	-17.16	-5.64	0.15
Mon	-3.75	-14.52	-14.18	-1.21
Tues	4.16	-27.76 **	-21.23 †	0.48
Weds	1.82	-27.58 *	-2.09	2.67 †
Thurs	4.98 †	-26.82 *	-34.09 **	-0.49
Fri	-5.55 †	35.39 **	45.54 **	1.67
Sat	-1.99	24.57 *	36.36 **	3.50 *
Sun	-2.34	-1.70	-13.67	-2.95 †
Mon	2.37	0.51	-3.67	-0.35
Tues	2.53	-6.61	-15.18	-2.51
Weds	5.71 †	—	—	—

* $p < 0.05$ ** $p < 0.01$ † $p < 0.10$ (trend)

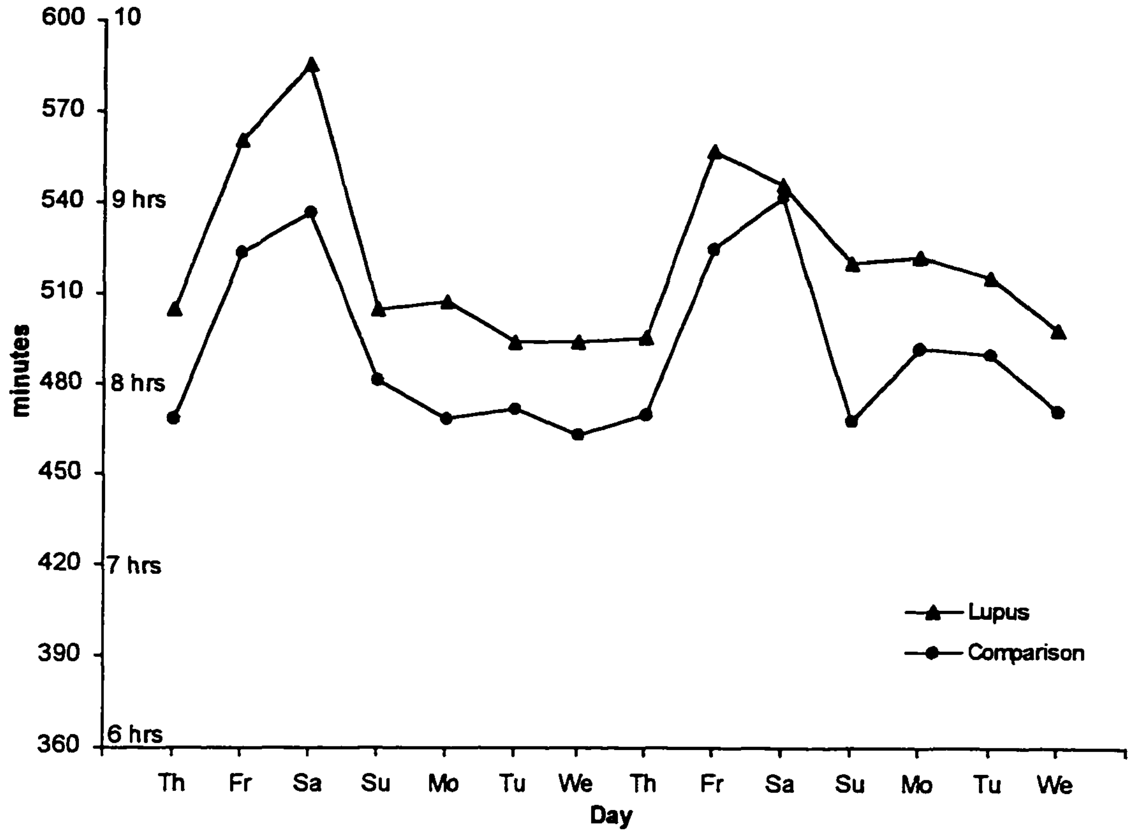
[a] Sleep ratings began on Thurs. night. Fatigue ratings began the next day, on Friday.

[b] Single degree of freedom tests and significance levels comparing each day's mean to the overall mean. Column values are unstandardized regression parameter estimates (beta). The sign indicates the direction of the difference between that day's mean and the overall mean across 14 days. The magnitude indicates the average amount of unit change in the variable predicted by that day's effect. Only 13 days of effects (k-1) are provided in the statistics output.

[c] Calculated based on time in bed trying to sleep (SE_SLP%).

Thursday) time in bed and a substantial increase on the weekends (Friday and Saturday) as illustrated in Figure 2. The day of week pattern was examined further in the lupus group in a one-way analysis of TIBTOT. A significant main effect of day emerged, and the single degree of freedom tests were examined. On both weekends of the diary, Friday and Saturday nights, TIBTOT was significantly longer than the overall mean for TIBTOT. Similarly, on three weeknights TIBTOT was significantly shorter than the overall mean. These day of week effects for TIBTOT are presented in Table 4.

Figure 2. Total Time in Bed



Daily total sleep time. In their baseline estimate of the past month's TST, women with lupus reported less TST than their peers (means: lupus= 382.53 mins.; comparison= 420.27 mins.; t(68) = -2.39, p = 0.02). In daily ratings, however, there was a group main effect to indicate women with lupus tended to get more TST. The groups' mean differences across the fourteen days were small, however, ranging from 0.23 to 22.07 minutes across the two weeks. While the statistical difference in TST seems unlikely given these mean differences; it is a function of error structure consistency, an issue discussed further at the end of the results section. To make some sense of these differences, the range of TST in each group is helpful. In the lupus group, the variability is not only higher, but the range of TST is wider. Minimum TST ranged from 179 min to 296 min; maxiumum TST ranged from 505 min to 647 min. Maximum TST values over 600 min occurred on six days. In the comparison group, however, minimum TST ranged from 207 min to 315 min; maximum TST ranged from 495 min to 595 min. So some women with lupus reported very little sleep, while others reported very long TST.

The TST data were best modeled with a banded autoregressive structure. The groups' patterns for nightly total sleep time are similar to those for time in bed, exhibiting a dramatic weekend increase followed by lower TST during the week (Figure 3). The day of week pattern was examined in the lupus group in a one-way analysis of TST. A significant main effect of day emerged, and the single degree of freedom tests were examined. On each Thursday night TST was significantly lower than the overall TST mean. On both Friday and Saturday nights, TST was significantly higher than the overall TST mean (Table 4).

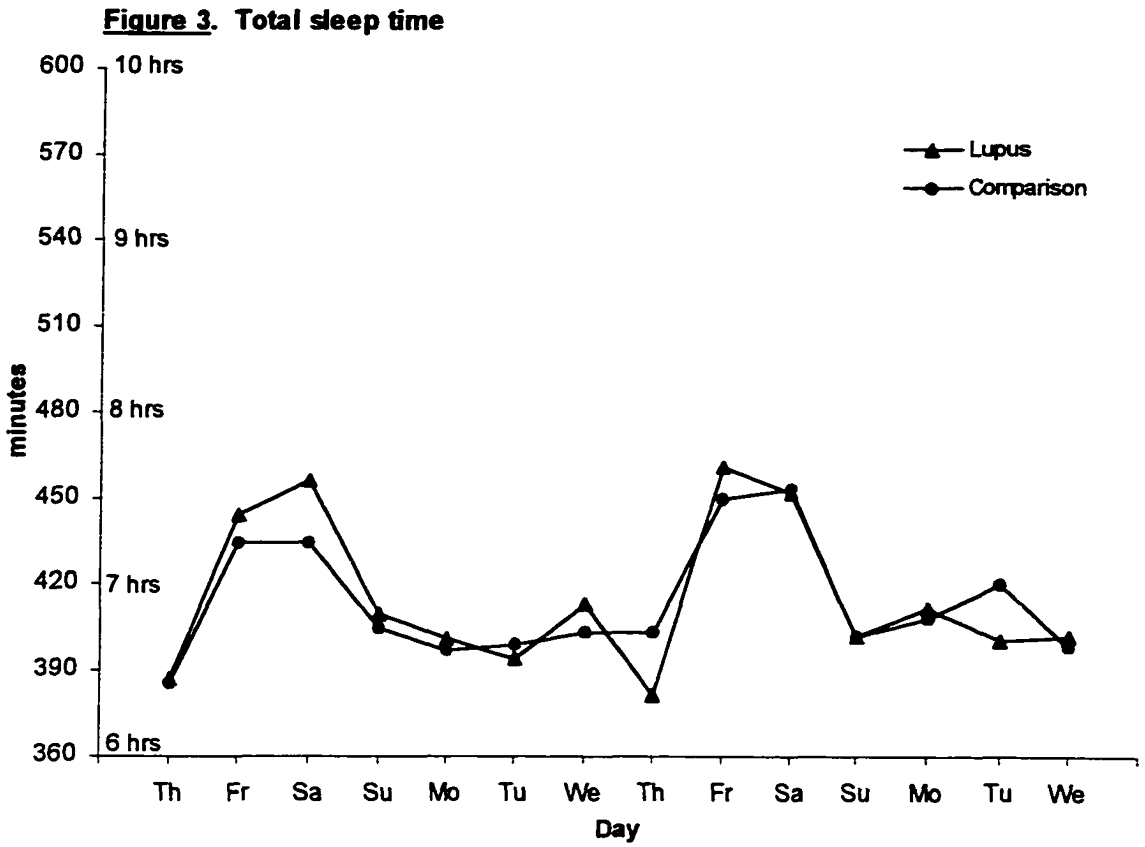


Figure 3. Total sleep time
600
570
540
510
480
450
420
390
360
10 hrs
9 hrs
8 hrs
7 hrs
6 hrs
minutes
Lupus
Comparison
Th
Fr
Sa
Su
Mo
Tu
We
Th
Fr
Sa
Su
Mo
Tu
We
Day

Sleep latency and wake time after sleep onset. At baseline, women with lupus estimated their typical sleep latency to be very high (means: lupus=33.09 mins.; comparison=13.57 mins.; $t(68) = 3.68$, $p < 0.001$). During the daily diary this difference was confirmed by a group main effect, but the average difference between the groups was not as great as the baseline estimate would have predicted. Group mean differences in SLAT ranged from 0.76 min to 12.78 min. Results for wake time after sleep onset were similar to those for sleep latency. The group main effect confirmed that the women with lupus reported greater amounts of time awake at night ($\chi2$ [1]= 15.33, p=.0001).

Night-to-night patterns of SLAT (Figure 4) and WASO (Figure 5) were not as cyclic as TIB and TST. Both of these distributions were modeled better by an unstructured covariance matrix, indicating that tonight's SLAT and WASO do not predict later nights' experiences. Although there were sizable fluctuations throughout the two weeks, there was not a regular pattern from night-to-night. As Figure 5 indicates, WASO increased substantially among the lupus group the second Sunday through Tuesday nights (nights 11-13).

Figure 4. Sleep latency

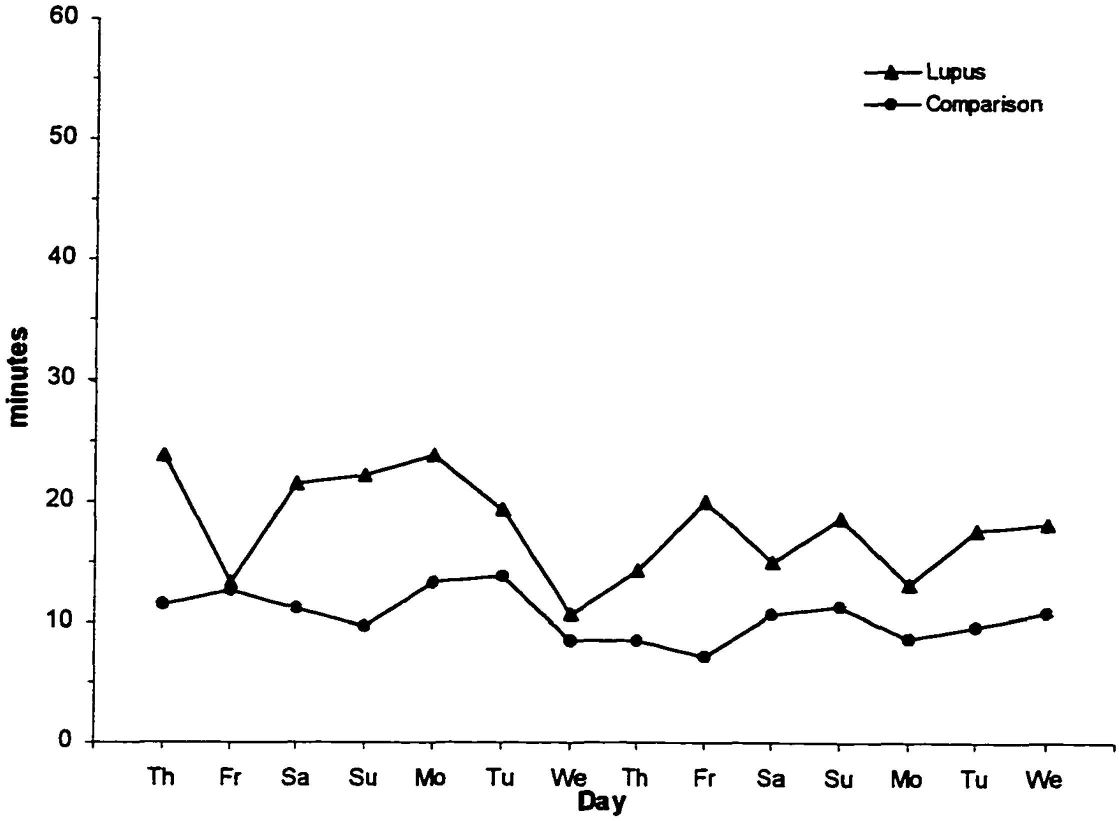
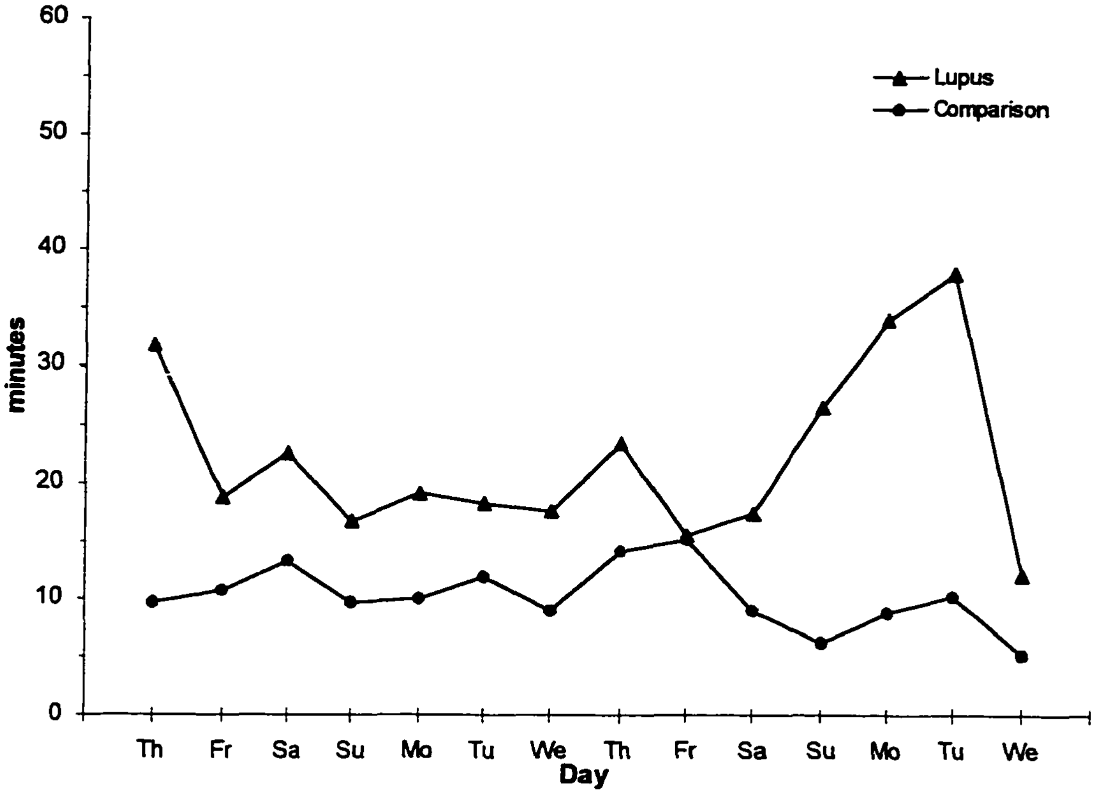


Figure 5. Wake Time After Sleep Onset



Sleep efficiency. Although the women with lupus reported getting slightly more TST than their peers, their SE_SLP% was lowered as a result of increased sleep latency and wake time after sleep onset. Differences in SE_TIB% did not reach statistical significance. Both sleep efficiency distributions were best modeled by an unstructured matrix probably due to the influence of SLAT and WASO, which also exhibited an unstructured form. Although the women increased both their TST and TIBSLP on the weekends, SE_SLP% did not reliably respond to these efforts. The day of week pattern was examined in the lupus group in a one-way analysis of SE_SLP%. A significant main effect of day emerged, and the single degree of freedom tests were examined. As expected given the unstructured matrix form of these data, the day of week effects showed no regular pattern. There were no reliable weekend changes in SE_SLP%. On the second weekend SE_SLP% increased significantly on Saturday night but decreased significantly on Sunday night. These day of week effects for SE_SLP% are presented in Table 4.

In analyses with raw score, rather than outlier-corrected, distributions there was no significant group difference in either SE_SLP or SE_TIB. Since Figures 6 and 7 suggest there were group differences in both forms of sleep efficiency, these weak findings may be due to error structure inconsistency between the groups. Further discussion of this issue appears at the end of the results descriptions.

Sleep quality. Women with lupus rated their nightly sleep quality (SQUAL) as poorer than the women without lupus, indicated by a group main effect. Daily patterns in SQUAL ratings were modeled by a banded autoregressive structure, although there was not a pronounced weekend effect.

Figure 6. Sleep efficiency (trying to sleep)

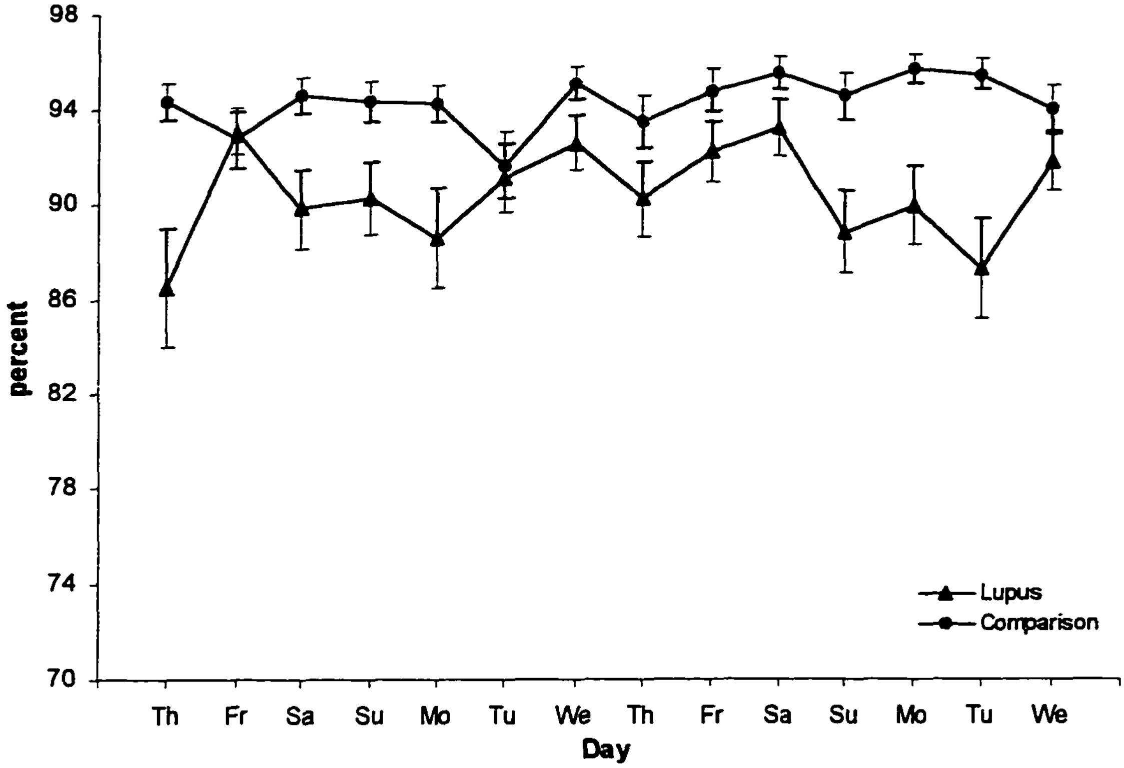
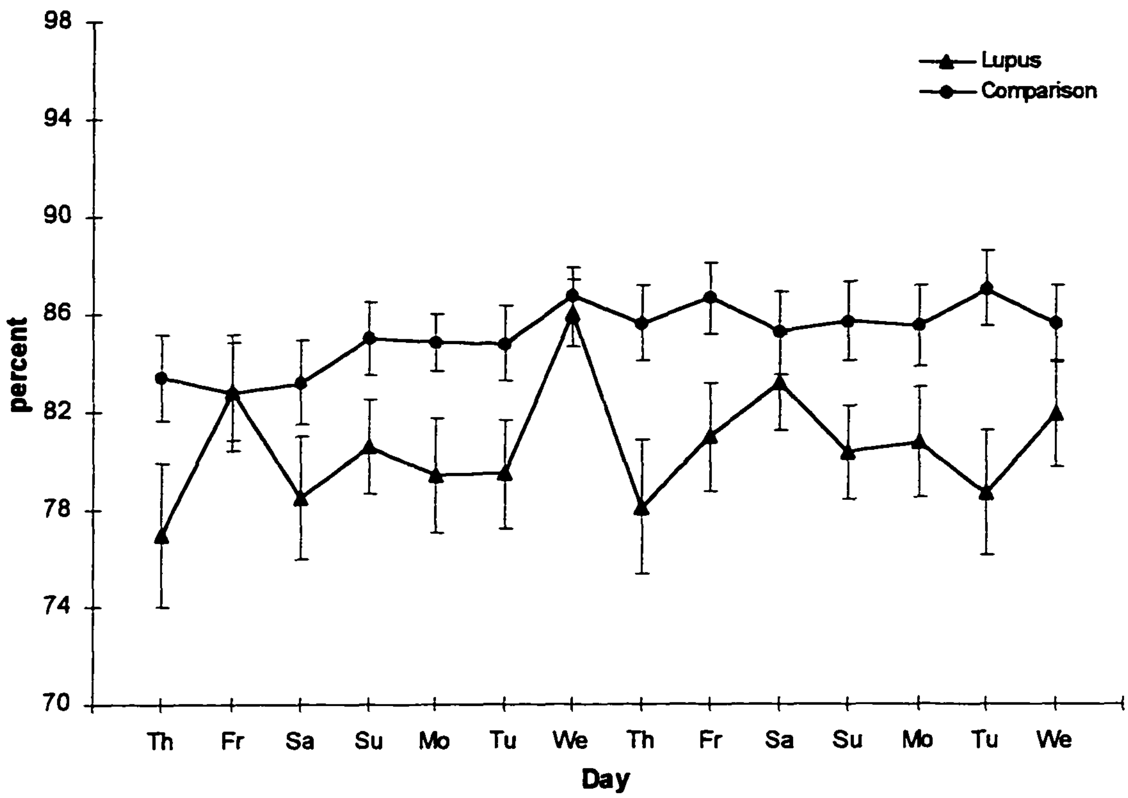


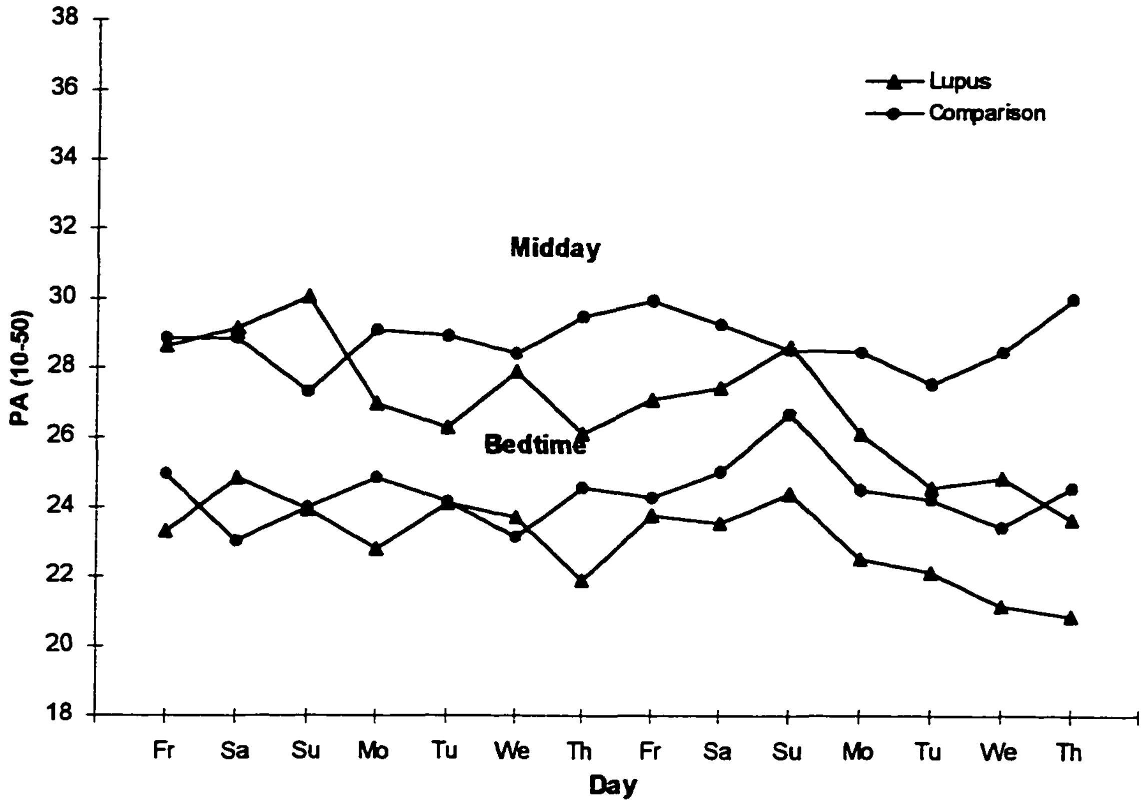
Figure 7. Sleep efficiency (time in bed)



Depressive symptoms and mood. Depressive symptoms assessed with the CESD were not different between the groups; however, there was a marginal trend for women with lupus to report lower depressive symptoms. Mean CESD scores for both groups were very stable over time.

On the positive affect scale of the PANAS, there was no significant group difference. There was a time of day main effect to indicate both groups reported higher positive mood during the day than at bedtime; however, there was no group by time of day interaction effect as there was for daily fatigue. The PA data were best modeled with a banded autoregressive structure (Figure 8); however, there was not a pronounced weekday–weekend cycle as there was for some of the sleep parameters. This is further confirmed by the lack of a day main effect for PA.

Figure 8. Midday and bedtime positive affect



A note on interpreting the results. Some of the significance levels in these results, notably those for TST, TIBSLP and SE_TIB% may seem unlikely given the relative group mean differences. For example, the group TST differences were very small but produced a significant main effect. Conversely, the TIBSLP differences appear large enough to be significantly different, as the TIBTOT differences were. These apparent discrepancies were likely a result of varying degrees of consistency in the error matrix structures across the analyses. A more consistent error matrix structure provides more power to detect a statistically significant difference between means whose absolute values may not be very different. The error structure consistency cannot be evaluated directly, but the variability, i.e. standard deviations, in the variables provides some clues about it. For most sleep variables the lupus group exhibited higher standard deviations than the comparison group, and across days their standard deviations fluctuated more. The degree of such inconsistency in the data differed across variables, thus affecting the error matrix structure consistency differently. The task in interpreting such seeming discrepancies is to judge the statistical significance of a finding against its potential clinical significance.

Discussion

Chronic fatigue is one of the most ubiquitous, yet difficult to manage symptoms in the rheumatic diseases and other chronic illnesses. In efforts to study fatigue, researchers too often conceptualize fatigue as a unitary construct. Greater emphasis is placed on identifying possible etiological factors for fatigue instead of exploring and describing the nature of the fatigue experience. Clinical experience and a growing literature in various populations suggest that "fatigue" may better be seen as a heuristic for a multidimensional phenomenon. Fatigue may be experienced in a variety of ways and may arise from numerous etiological pathways. In this study the focus is on fatigue among women with lupus. The main premise of this paper is that more elaborated descriptions of both fatigue and potential etiological factors for fatigue in lupus are needed for two reasons. First, better descriptions of fatigue phenomenology and time course not only will help care providers be more sensitive to patients' experience, but also will help identify effective ways to manage fatigue. Second, better description of factors thought to contribute to fatigue will help elucidate these factors' causal relationships to fatigue.

Fatigue severity and temporal characteristics in daily life. Drawing on work by Piper (Piper, 1989; Piper et al., 1989), this study measures fatigue along several dimensions in an attempt to disentangle underlying components and meanings. Factor analyses of the Piper subscales suggest that in the lupus population fatigue is indeed a multifaceted construct. Two of the dimensions addressed in the PFS, fatigue severity and temporal course, are also assessed through a daily diary methodology. Most researchers have found that people with rheumatic disease report greater fatigue severity and more chronic fatigue than people without rheumatic disease (Belza, 1995; Knippen, 1988;

Krupp et al., 1989). The results in both the cross-sectional study (McKinley et al., 1995) and this daily study suggest that fatigue's severity and temporal course may be intimately linked in affecting the subjective appraisal of fatigue.

On the PFS temporal dimension subscale, higher ratings generally indicate fatigue tends to be chronic, continuous (without breaks), and has increased during the past week. Contrary to the cross-sectional results, in weekly ratings these temporal aspects of fatigue are not different for women with lupus. In both studies, subjective fatigue severity on the PFS is only marginally higher for women with lupus. Similarly, overall daily fatigue severity is not different among the lupus group. Across 14 days, however, fatigue is fairly consistently higher during the day for the women with lupus. Both groups of women exhibit a day-to-day cyclicity in fatigue. Fatigue this afternoon affects somewhat an individual's fatigue both tonight and tomorrow afternoon. Both daytime and nighttime fatigue tend to rise and fall over the course of two or more days (Figure 1). Part of this cyclicity is linked to a decrease in fatigue on the weekends.

These findings may have implications for the way women perceive both the severity and chronicity of fatigue. Most people experience diurnal fatigue fluctuations, and by mid-afternoon fatigue tends to be rising (Monk et al., 1985; Thayer, 1989). Consistent with these typical patterns, both groups in this study reported higher fatigue at bedtime than during the day. In this study the PFS provides a weekly snapshot of fatigue now, or during the past 24 hr; however, it was completed near bedtime. The bedtime peak of fatigue may have contributed to the lack of differences on the PFS severity ratings. The time of day findings may also inform perceptions of fatigue chronicity. If this window of 14 days is representative, the findings indicate that women with lupus perceive their daytime fatigue chronically to be higher than their peers. Fatigue ebbs and flows day to day, however, so there are times of relatively less fatigue. When asked on the PFS to what degree their current, i.e. bedtime, fatigue represents a chronic, continuous experience, the groups do not differ. This may be somewhat a limitation of the PFS in focusing only on fatigue at the moment. It also suggests that women perceive the diurnal and daily variations to represent a less chronic form of fatigue than if fatigue were more stable day-to-day or within each day. Another factor contributing to this perception may be disease activity status. There are no published studies describing fatigue during severe flare periods, but clinical anecdotes provide some certainty that fatigue is worst during such times. Most participants were experiencing mild to moderate disease activity. As a result, fatigue might have been perceived as more transient than the fatigue associated with major disease flare episodes.

On the other hand, the ongoing elevated daytime fatigue may help explain the descriptive reports that people with lupus find fatigue so debilitating (Knippen, 1988; Liang et al., 1984; Ouellette et al., 1989; Robb-Nicholson et al., 1989). A similar diurnal fatigue pattern has been demonstrated in RA (Stone et al., 1997). In that study only 34% of participants experienced diurnal fluctuations, suggesting that others experience more stable fatigue patterns. Those with and without diurnal fatigue patterns were compared but were not different on ratings of fatigue severity, joint and muscle pain and stiffness, and sleep quality. It would be useful to explore further how daily and diurnal fatigue variability affects women's perceptions of fatigue's severity and chronicity. Time of day fatigue variations may be important in managing fatigue. Individuals can map their own daily fatigue patterns, identify low and high fatigue times of day, and plan activities as strategically as possible around one's daily pattern.

Descriptive dimensions of fatigue. Several other fatigue dimensions measured with the PFS may help define lupus fatigue. Part of Piper's original fatigue severity subscale seems better characterized as fatigue consequences, or functional impact. In chronic illness populations, functional status measures are important indicators of disease impact, treatment outcome and quality of life. While the lupus group did not rate fatigue severity higher overall, they did report more limitations in various activities due to fatigue. This finding may be related to time of day and daily fatigue variations, as discussed above. Elevated fatigue early in the day is more likely to interfere with work and other responsibilities. These women are maintaining work and family responsibilities similar to their peers', but daytime fatigue may make it much harder for them to do so. The mean score on this fatigue consequences scale was not especially high, but further psychometric work is needed to know how to evaluate the absolute scores. It would be worthwhile to explore how this measure relates to other functional status indicators. One potential limitation of this scale is that the items require an attribution about fatigue causing the functional limitation (e.g., to what degree has fatigue interfered with your ability to complete your work). A rating of causal attribution is confounded with a rating of functional limitation. It would be useful to disentangle these ratings to determine the impact of fatigue level on functional status. Generally, however, this group difference confirms that women perceive fatigue having a more pronounced impact than do women who do not have lupus.

On the PFS affective component, women with lupus also perceived fatigue as a more negative experience overall. One difficulty in identifying the fatigue components most salient for chronic illness populations is that fatigue is ubiquitous. Everyone experiences it as part of normal life. In the general population fatigue arises under various conditions due to various causes. Because fatigue is usually associated with physical or mental exertion, has limited duration and remits after rest or sleep, it is commonly perceived as a recuperative, homeostatic process (Piper, 1989). Fatigue is also a common complaint by people seeking primary medical care (Fuhrer & Wessely, 1995; Kroenke, Wood, Mangelsdorff, Meier, & Powell, 1988). In the majority of these cases, fatigue is associated with an identifiable medical or psychological disorder. For example, acute medical conditions such as influenza infections are usually accompanied by severe fatigue which remits along with the other clinical symptoms. Fatigue is a common side effect of major surgery or chemotherapy. Generally, fatigue is only considered problematic when it becomes functionally debilitating, chronic or arises from unclear causes. Lupus fatigue often meets all three of these conditions. The affective subscale of the PFS addresses some of the more affect-laden attributions people may make about their fatigue experience. In this study women with lupus tended to view their fatigue as a more negative, abnormal, unpleasant phenomenon, rather than a normal, homeostatic mechanism.

In the rheumatic disease literature, the sensory experience of fatigue has not been described. Pain research has shown that the sensory experience of pain varies along a number of dimensions (Melzack, 1975). Piper addressed fatigue sensation in developing her scale (Piper et al., 1989). In this study, factor analytic results suggests that fatigue may subsume several types of phenomenology. Fatigue is partially felt as tiredness, which includes a sense of low energy, sluggishness and weakness. These states are commonly associated with fatigue. Additional feeling states associated with fatigue may be more aptly characterized as sleepiness, cognitive difficulties, anxiety and motivation. While these categories were derived based on data from the lupus group, they appear relevant to the experience among women who do not have lupus, as well. The groups do not differ on any of these sensory aspects of fatigue; however, the scores in both groups suggest the measures are salient to their experience. For example, these measures were completed around bedtime, and mean scores on the tiredness and sleepiness subscales are appropriately elevated relative to group means on the other PFS subscales. This sensory component also did not differ in the cross-sectional study reported in chapter 2.

It is somewhat surprising that none of these dimensions differentiated the groups. One obvious potential reason is that the measures were completed at the end of the day. Some of these sensory components of fatigue are likely subject to the diurnal variation observed for more general fatigue ratings (Monk et al., 1985; Stone et al., 1997); therefore, the bedtime ratings likely assessed peak times for them in both groups. The cognitive functions addressed with this measure are primarily attention, memory and general cognitive fluency. The prevalence of some types of cognitive deficits, thought to ensue from CNS involvement of the disease's inflammatory processes, is relatively high in lupus (Carbotte, Denburg, & Denburg, 1986; Shapiro, 1997). In lupus, fatigue has been correlated with cognitive deficits measured through neuropsychological batteries (Denburg, 1997), but the PFS measure did not indicate higher perceived cognitive difficulties among the lupus group. This finding is likely due to low sensitivity in this PFS subscale; it may also reflect women's reticence to endorse the cognitive items too highly because they know about the possible CNS effects of the disease.

Regarding the course of these fatigue dimensions over time, one consistent trend emerges. For each of these dimensions, ratings one week predict ratings the next week, as indicated by a first order autoregressive structure. These trends indicate that an individual's ratings on these dimensions are somewhat related and consistent over time. Whether this relationship extends beyond a one-week lag could not be explored because only three time points were assessed. In fact, confidence in a one-week lag would be increased by measuring these dimensions over more than three time points to confirm the consistency of this trend.

Exploring these dimensions indicates that lupus fatigue likely involves several components. These components may variably distinguish lupus fatigue from fatigue in the general population depending on different time frames, contexts and lupus disease activity levels. In this study women with lupus perceive fatigue as a problem, as indicated in the affective and fatigue consequences scales, and the trend toward greater fatigue severity ratings. Given the time of day differences and methodological considerations discussed earlier, it would be worthwhile to explore these dimensions further. The dimensions addressed here may not fully represent the range of fatigue experiences. Using the PFS or similar quantitative measures should not be the only approach to defining fatigue dimensions. Further descriptive exploration, including a more qualitative approach, is needed for understanding the fatigue experience of people with lupus.

Nightly sleep patterns in lupus. In this study self-reported sleep patterns in lupus generally concur with reports in other rheumatic disease groups. The results suggest a substantial prevalence of sleep initiation and maintenance problems. As a result, the women experience their sleep as less refreshing and satisfying than their peers. While such self-reports are not as quantitatively accurate as polysomnography records, data from the two methods are usually well correlated (Frankel, Coursey, Buchbinder, & Snyder, 1976; Hirsh et al., 1994). Unlike sleep lab recordings or retrospective subjective reports, daily sleep diaries offer a more detailed, naturalistic view of typical sleep patterns and personal habits that may contribute to these patterns. The group differences in sleep may also inform the findings for fatigue.

The women with lupus report more difficulties with sleep both in terms of initiating sleep (sleep latency) and maintaining consolidated sleep during the night (wake time after sleep onset). People with lupus express a lot of concern with getting enough sleep (Ouellette et al., 1989; Robb-Nicholson et al., 1989). The lupus group's retrospective baseline estimate of average total sleep time is much lower than the comparison group's. In the daily data, the scenario is much different. Statistically the lupus group reports slightly more nightly total sleep time than the comparison group. The clinical relevance of these findings depends more on descriptive features of the groups' distributions. There is considerable variability in TST for both groups, so a substantial number of women in both groups are getting less sleep than the means in Figure 3 suggest. In addition, the range of TST is considerably wider in the lupus group. Some women report very long nightly sleep times. These extremes of very long and very short sleep times in the lupus population should be explored further. Overall, the mean amount of sleep in both groups is somewhat low during the week. Individuals certainly vary in their typical sleep need, but the mean for both groups is less than seven hours during the week. Healthy women may habitually get by with this amount, but for women with lupus who perceive a need for plenty of sleep and have trouble with daytime fatigue, overall total sleep time may be too low. This conclusion is speculative, however, and warrants further research and clinical investigation in the lupus population.

In this study women with lupus tend to spend more time in bed trying to sleep, but the group difference is not significant. They habitually spend more total time in bed than their peers, however. The women with lupus routinely add considerable rest time in bed before sleeping at night and after awakening in the morning. The time in bed measures in this study are less fine grained than the measure typically derived from sleep diaries, which ask respondents to record all episodes of getting out of bed during the night, then returning to bed to try to sleep. Nevertheless, these measures point reliably to a tendency for the women with lupus to allow more time in bed than their peers. The sleep efficiency ratio summarizes the balance among time in bed, time spent asleep, and time spent awake while trying to sleep. Sleep efficiency based on the time in bed between lights out and morning awakening is lower among the lupus group. Sleep efficiency based on total time in bed is not significantly different, even though the groups look very different in Figure 7. As explained in the results section, the group difference in SE_TIB% may be masked by higher variability in the lupus group, contributing to a more inconsistent error structure in the analysis.

In terms of behavioral sleep management, time spent in bed is an important parameter affecting sleep efficiency. People with insomnia often lie in bed unable to sleep and spend that time watching the clock, trying too hard to sleep, and becoming worried about not being able to sleep. They may also lengthen their total nightly time in bed in an effort to get more sleep (Hauri & Fisher, 1986; Spielman & Glovinsky, 1997). Eventually a conditioned association develops between being in bed and not being able to sleep, and this pattern serves to perpetuate the insomnia by propagating both sleep onset and maintenance disruptions, thus lowering sleep efficiency. Clinically, one is usually most concerned with the time in bed trying to sleep, between turning out the light at night and awakening in the morning. If sleep is disrupted during this period, but the individual stays in bed trying to sleep rather than getting out of bed, efforts to sleep are often thwarted.

In these results, however, the lupus group's habit of spending extra bed rest time around the sleep period is also cause for concern. Responding to open-ended questions in the weekly questionnaires, these women frequently mention using rest as a fatigue management strategy. Many find reclining in bed provides some relief from joint pain and other symptoms, so they get into bed at night to read, pay bills, catch up on work, or socialize with their family. As one woman pointed out, living in a small urban apartment often means that the bed is the only comfortable seating in the home. Adding such time in bed may promote negative conditioning between bed and sleep in much the same way that tossing and turning during the night does. Also, some of this bed rest time is likely spent dozing or sleeping, but these times are not always accurately represented through the subjective reports. For example, those who read or watch television in bed often fall asleep, awaken and get out of bed to complete their evening chores or bedtime routine, then return to bed to sleep. Such behavior can foster longer sleep latency, as well as less consolidated sleep during the night.

Another important feature of the total sleep time and time in bed results is the similarity of the weekly sleep patterns in both groups. The banded autoregressive pattern found in these data reflect this pattern, and it is dramatically represented in Figures 2 and 3. Both groups reduce their total sleep time and time in bed during the week in the service of other activities, then add considerably more time in bed on weekends. This pattern is a common sleep habit for those on a typical five-day work week. For healthy individuals whose sleep efficiency is not compromised, the weekend catch-up strategy may provide enough restoration to function adequately. For people with lupus, who are having trouble with fatigue and experiencing reduced sleep efficiency due to longer SLAT and WASO, catching up on weekends may not be sufficient. Among the lupus group, the extra weekend time in bed successfully allows them to increase their total sleep time. Their sleep latency, wake time during the night, and consequently, sleep efficiency do not correspondingly increase on the weekend, however. These indices of sleep quality fluctuate on a more random basis than time in bed and total sleep time. From a clinical sleep hygiene perspective, keeping an irregular weekday—weekend sleep schedule, in conjunction with spending too much time in bed may be fostering the lupus group's disrupted, less efficient sleep (Hauri & Fisher, 1986; Spielman & Glovinsky, 1997; Spielman et al., 1987).

Mood and depressive symptoms. The findings for prospectively assessed depressive symptoms and mood concur with the cross-sectional study results. In the prior study depressive symptoms on the CESD did not differ between women with lupus and a well-matched group of women without lupus. In this study with weekly CESD assessments, depression ratings again do not differ. On the contrary, the women with lupus tend to rate depressive symptoms slightly lower than their peers. In addition, the percentage of women scoring above the CESD criterion for depression is not higher between the groups. There are few reports on depression in lupus with which to compare these findings. In one study of clinic patients, people with lupus scored higher on the CESD than non-patient healthy volunteers but not higher than patients with multiple sclerosis. In that study the percent of participants scoring above the CESD criterion for depression (≥ 16) was 39% for lupus, 48% for multiple sclerosis and 15% for healthy controls (Krupp et al., 1989). A similar percent of those scoring above the CESD criterion, 39% of lupus patients, was found in the aerobic conditioning study cited earlier (Robb-Nicholson et al., 1989). Knippen reports high scores on the CESD in her study sample. Their mean score was 20.85 (std dev=8.68). She reports 73% of the sample had depressive symptomology, which presumably is based on the same criterion score of 16. Many participants in her study were also enrolled in a research protocol for lupus nephritis treatment, thus they likely were experiencing more severe disease activity than the women in this study. Among women with lupus in this study, the rates for scoring above this CESD criterion are lower than all the above studies, at 21.21% and 24.24% across the three weekly time points.

Of greater interest in this study are the daily experiences of depressive mood and how daily mood may be related to daily fatigue. As with the CESD, daily mood ratings do not differ between the groups either at midday or bedtime. As expected, both groups of women report more positive mood during the day than at bedtime, so in this respect mood parallels fatigue. As fatigue increases later in the day, mood worsens. Overall, however, the daily mood patterns do not parallel closely the daily fatigue patterns. Daily mood exhibits a banded autoregressive cyclicity, but there is not a strong weekend–weekday trend as in fatigue and some of the sleep variables. Further, the two groups' daily mood fluctuations appear not to closely parallel each other; however, there was not a group by day interaction effect to confirm this.

In many ways the lack of group differences in mood is not so important as the relationship of mood to other factors. The relationship of depressive symptoms and mood to disease activity, functional status and other variables has been investigated in other rheumatic disease groups, primarily RA. The methodologies and findings vary considerably. When depression is studied as the outcome, disease-related variables can contribute significantly to its occurrence (Newman, Fitzpatrick, Lamb, & Shipley, 1989; Wolfe & Hawley, 1993); however, demographic and socioeconomic variables often predict depression equally if not more strongly than disease variables (Hawley & Wolfe, 1988). When depression is studied as a predictor variable, it can contribute to increased pain, fatigue (Fifield, Tennen, Reisine, & McQuillan, 1996), functional outcomes, health services utilization, and other disease activity indicators (Katz & Yelin, 1993). Drawing from this literature, it would be helpful to explore some of these same relationships in the lupus population.

In summary, these findings illustrate that people with lupus may perceive fatigue as so troublesome because it increases too early in the day, thereby interfering with various important activities. Fatigue does fluctuate day-to-day, and this feature of fatigue may enhance its negative impact. Consequently, the phenomenological experience of fatigue in lupus is distinguished more along an affective dimension than a sensory one. The results also show that sleep difficulties are common, as in other rheumatic disease groups. Some of the sleep disruption may be related to poor sleep habits, such as spending too much time in bed and keeping an irregular daily sleep schedule. The next step in this research program is to investigate how daily trends in sleep, mood and fatigue may be related. In the study reported in Chapter 2, an explanatory model of fatigue was proposed and tested with cross-sectional data. The model explores how lupus disease activity, depressive symptoms and sleep quality interrelate to affect fatigue. Depressive symptoms were shown to mediate the effects of disease activity on fatigue. Sleep disruption and anxiety about sleep also mediated the effects of disease activity on fatigue. Finally, sleep and depression were found reciprocally to predict each other, suggesting that sleep disruption and mood disturbance can perpetuate each other and, potentially, perpetuate fatigue. These findings imply that interventions addressing sleep and mood may be helpful in relieving fatigue. The suggested relationships are complex, however, and should be studied with a more process-oriented approach. In the next chapter this model of fatigue is tested using the prospective, daily data from this study.

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Chapter 4

The Contributions of Pain Symptoms, Sleep Quality and Depressed Mood to Fatigue in SLE: Replicating a Mediational Model Using Daily Measures

People with systemic lupus erythematosus (lupus) describe fatigue as one of the most debilitating symptoms associated with their disease (Krupp, LaRocca, Muir, & Steinberg, 1990; Liang et al., 1984; McCoy, Callahan, & Pincus, 1992; Robb-Nicholson et al., 1989). Fatigue is a difficult symptom to treat, however, because the etiology of fatigue in lupus is unknown. Fatigue is a nonspecific symptom of lupus (Lahita, 1997; Wallace, 1997) and is not objectively defined or measurable. Consequently, standard medical treatments to control lupus disease activity are not widely effective for fatigue (Hahn, 1997). Fatigue is a ubiquitous problem in a variety of conditions and populations. Increasingly, researchers in various disciplines recognize that fatigue is likely a complex phenomenon affected by psychological, social and cultural, as well as physiological factors (Aarons, Forester, Hall, & Salmon, 1996; Belza, Henke, Yelin, Epstein, & Gilliss, 1993; Chen, 1986; Fuhrer & Wessely, 1995; Lewis & Wessely, 1992; Piper, 1989; Sternberg, 1993). We may learn more about fatigue etiology in lupus by looking to what is known generally about fatigue, rather than trying to define an etiology unique to lupus.

Drawing on existing theory, research and clinical interventions in other populations, I have proposed an explanatory model of lupus fatigue. The model (Figure 1) posits that fatigue is a product of lupus disease manifestations, decreased sleep quality, and depressive symptoms and mood. These variables or related ones have been shown to be independently related to fatigue in other rheumatic disease groups (Affleck, Tennen, Urrows, & Higgins, 1992; Anch, Lue, MacLean, & Moldofsky, 1991; Belza et al., 1993; Crosby, 1991; Jennum, Drewes, Andreasen, & Nielsen, 1993; Mahowald, Mahowald, Bundlie, & Ytterberg, 1989; Moldofsky, 1993). The main purpose of this model, however, is to investigate multifactoral processes underlying fatigue. Rather than assessing independent effects on fatigue, the interrelationships among these factors may reveal more about fatigue etiology. In this model sleep and mood are proposed to be mediators or mechanisms through which disease activity increases fatigue. More specifically poor sleep quality and depressive mood are proposed to help perpetuate each other through a reciprocal causal process (paths A1 and B1 in Fig. 1), and this process is a mediational mechanism through which lupus disease manifestations contribute to fatigue. This model is specific to lupus fatigue in identifying disease activity as the precipitating or perpetuating cause, not only of fatigue, but also of sleep disruptions and mood disturbance. The rest of the model, however, represents processes that can affect fatigue in other populations.

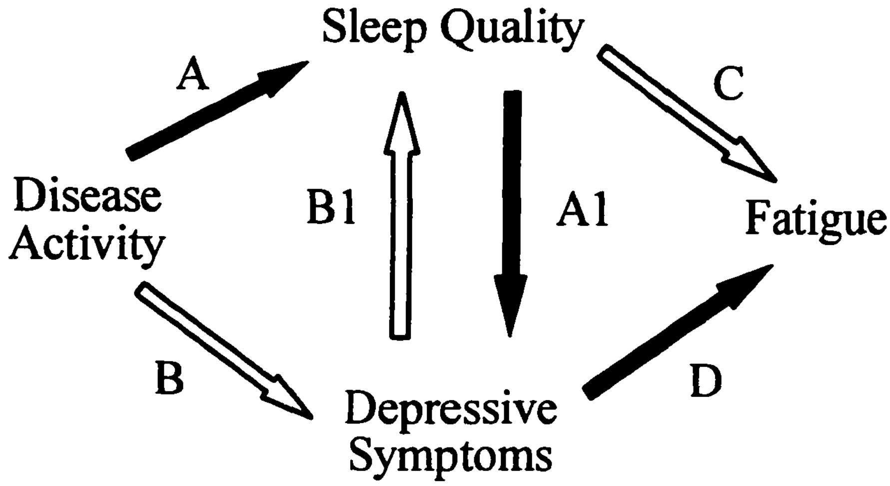

Figure 1. Proposed mediational model of fatigue in lupus.

Time frames for studying fatigue. This model was introduced and tested with cross-sectional data in a prior paper (McKinley, Ouellette, & Winkel, 1995) (chapter 2). The results generally supported the model, but prospective data are needed to test adequately the directional, interrelated processes as they are proposed. While this is an etiological model, it is not considered a comprehensive explanation of lupus fatigue. Instead, the overarching goal influencing this model's structure has been to identify viable intervention strategies for fatigue. Toward that goal, a vital consideration is the clinically relevant time frames within which fatigue has the most impact. In lupus and other rheumatic diseases, salient fluctuations in fatigue likely occur in diurnal, daily and weekly time frames. Disease activity does correlate generally with fatigue (Wysenbeek, Leibovici, Weinberger, & Guedj, 1993), thus fatigue is probably at its worst during severe disease flare periods. The few descriptive studies of lupus fatigue suggest that people with lupus also find fatigue troublesome in everyday life when disease activity is relatively low (Krupp et al., 1990; Liang et al., 1984; McCoy et al., 1992; Robb-Nicholson et al., 1989). Stone and colleagues described diurnal fatigue cycles in people with rheumatoid arthritis (RA) (Stone, Broderick, Porter, & Kaell, 1997). Daily patterns in lupus fatigue, presented in chapter 3, indicated fatigue is consistently higher during the day for women with lupus than for women without lupus. Fatigue was not stable among the lupus group; however, it fluctuated day-to-day.

This study replicates and extends the model results reported in chapter 2 using prospective, daily data from a fourteen-day diary. There are three components, or hypotheses, comprising this model. First, lupus disease activity, sleep quality and depressive mood independently are expected to affect daily fatigue over time. Second, daily sleep quality and depressed mood are expected reciprocally to affect each other over time. This hypothesis specifically predicts that sleep affects later mood, and mood affects later sleep. Third, daily sleep quality and depressed mood are expected to mediate the effects of lupus disease activity on daily fatigue. A few researchers have begun using daily events methodologies to study these variables or related ones among rheumatic disease populations. This daily process literature and other research and theory relevant to these three components of the proposed model are reviewed below.

Do lupus disease symptoms, sleep quality, and depressed mood affect daily fatigue? The frequency and time course of lupus disease symptoms has not been described. One group reported the effects of daily stress on lupus symptoms (Adams, Dammers, Saia, Brantley, & Gaydos, 1994). They reported only descriptive statistics collapsed over 56 days, rather than describing daily trends; nevertheless, these summary data suggested that lupus symptoms do fluctuate considerably over a short time. There are no reports linking lupus symptoms to daily fatigue. Fatigue has been correlated generally with increased lupus disease activity (Knippen, 1988; Wysenbeek et al., 1993), but not reliably with specific signs or symptoms. In a seven-day study of rheumatoid arthritis (RA), daily pain severity and variability were associated with both daily fatigue severity and variability (Stone et al., 1997). Some have argued that lupus fatigue is explained by comorbid fibromyalgia, rather than lupus disease activity per se (Petri & Steckroth, 1996). In that study some of the fibromyalgia symptoms associated with fatigue are also common in lupus: generalized aches and pains, headaches, joint stiffness, and paresthesias. These results do not convincingly argue that lupus symptoms have no impact on fatigue. They may, however, support the hypothesis that sleep quality affects lupus fatigue. If comorbid fibromyalgia does enhance fatigue for people with lupus, the sleep fragmentation usually accompanying fibromyalgia is likely one reason.

The prevalence of fatigue in lupus, as high as 80-100% (Schur, 1993; Wysenbeek et al., 1993), implies a substantial prevalence of sleep disorders. Fatigue, in the form of both physical lethargy and cognitive speed or fluency problems, is commonly associated with both the insomnias and sleep-fragmenting disorders such as periodic limb movements and sleep apnea (Spielman & Glovinsky, 1997; Stepanski, Lamphere, Badia, Zorick, & Roth, 1984). Experimentally induced sleep fragmentation, even without substantially decreased total sleep time, can also produce fatigue and related states (Bonnet, 1985; Bonnet, 1989). There are no published polysomnography studies in lupus, but subjective reports suggest people with lupus often experience disrupted, unrefreshing sleep (Knippen, 1988; Robb-Nicholson et al., 1989). The daily data presented in chapter 3 suggest many women with lupus keep irregular sleep–wake schedules and feel the need to catch up on sleep during the weekends. These are common habits – the comparison group followed similar patterns – yet they may indicate an existing sleep deficit or insomnia (Spielman & Glovinsky, 1997; White & Mitler, 1997). A high prevalence of severe sleep fragmentation, sleep apnea and periodic limb movements, but not altered sleep architecture, has been documented in several studies of RA (Crosby, 1988; Hirsh et al., 1994; Mahowald et al., 1989). Sleep findings in fibromyalgia are similar, and these studies have more explicitly confirmed an association between sleep and fatigue (Anch et al., 1991; Jennum et al., 1993; Moldofsky, 1993; Moldofsky, Scarisbrick, England, & Smythe, 1975). There are no reports describing the relationship between sleep and fatigue among people with lupus.

Despite widespread interest in depression and the concurrence of depression and fatigue in fibromyalgia, there has been almost no research directly linking mood and fatigue in rheumatic disease populations (Aaron et al., 1996; Hawley & Wolfe, 1988; Petri & Steckroth, 1996; Yunus & Aldag, 1996). The relationship of depression and general mood states to fatigue is an important aspect of mood theory which could be helpful in understanding lupus fatigue. Physical lethargy and cognitive sluggishness, often associated with fatigue, are markers of most major depressive disorders (Association, 1994). On a more normative level, mood is generally defined as two independent, bipolar dimensions. The dimensions are usually labeled positive and negative affect (PA and NA) (Watson, Clark, & Tellegen, 1988; Watson & Tellegen, 1985); or the analogs energetic and tense arousal to refer to associated physiological arousal states (Thayer, 1989). Positive affect is defined generally as active, pleasurable engagement and alertness, whereas NA is defined generally as subjective distress and dissatisfaction. Low PA is associated with fatigue-related states, including cognitive and physical sluggishness, decreased concentration, and sleepiness. PA is more purely associated with depressed affect, whereas NA contains components of both anxious and depressed states (Watson & Kendall, 1989). Thayer makes the link between PA and fatigue more explicit in describing the interface between mood and physiological arousal states (Thayer, 1989). Positive affect, thus, is the mood dimension more closely related to fatigue. PA reliably exhibits diurnal fluctuation patterns (Clark, Watson, & Leeka, 1989; Monk, Fookson, Moline, & Pollak, 1985; Thayer, 1987). Peak PA times of day vary across studies, due partially to methodology and to individual differences in peak PA times. Nevertheless, PA tends to peak between noon and mid-afternoon (Thayer, 1989). Daily PA levels and fluctuations should be somewhat related to one's experience of daily fatigue.

Do sleep quality and depressed mood reciprocally affect each other? The association between major depression and certain sleep characteristics is well known (Kupfer, 1995). The causal direction of this association is uncertain, (Moffaert, 1994), but there is evidence to suggest that sleep and depression affect each other, or that both are linked to a common etiological factor (Borbély & Wirz-Justice, 1982; Janowsky, El-Yousef, Davis, & Sekerke, 1972; Kerkhofs, Linkowski, Lucas, & Mendlewicz, 1991; Kupfer, 1995). On a more normative level, minor, short term sleep disruption can impair mood (Bonnet, 1985; Bonnet, 1989). Clinicians routinely use daily sleep diaries as diagnostic tools (Spielman & Glovinsky, 1997). Paradoxically, sleep researchers rarely use daily diary methods to study causal influences on sleep, or outcomes affected by sleep fluctuations. In one exception, Totterdell and colleagues studied sleep, mood and health symptoms for fourteen days in nondepressed volunteers (physical health status was not reported). Tonight's sleep latency, sleep onset time, awakenings during the night and perceived sleep quality affected tomorrow's positive mood. Reduced sleep quality also predicted cognitive symptoms which might be associated with depressed mood (trouble with memory, concentration, decisions, etc.). Today's positive mood affected only tonight's number of awakenings; however, the cognitive symptoms ratings also predicted number of awakenings (Totterdell, Reynolds, Parkinson, & Briner, 1994). These findings suggest bidirectional relationships between sleep and mood. Both sequences, sleep–mood and mood–sleep, would need to be tested simultaneously to confirm directly the bidirectional effects. There are no daily studies addressing the sleep–mood relationship in rheumatic disease. Nicassio and Wallston reported sleep, mood and pain relationships over 24-month intervals in RA. Pain and the interaction of pain and sleep problems predicted depressive symptoms concurrently and two years later. In the reverse direction, pain but not depression predicted sleep two years later (Nicassio & Wallston, 1992).

Do sleep quality and depressed mood mediate the effects of symptoms on fatigue? Conceptually a mediator is a mechanism through which one variable affects another. Only if lupus symptoms directly disrupt sleep and mood could sleep and mood, as mediators, consequently increase fatigue. The effects of disease activity on sleep and mood have not been studied in lupus, nor have daily relationships among these variables been studied widely in other rheumatic disease groups. Using both between-persons and within-persons analyses among RA patients, Stone and colleagues found daily pain and fatigue were related to last night's perceived sleep quality; fatigue was not related to last night's total sleep time in RA (Stone et al., 1997). These authors did not address whether pain affects subsequent sleep. Among women with fibromyalgia, Affleck, et al. showed relationships in both directions between nightly sleep quality and daily pain intensity, but not when controlling for attention to pain. Conversely, bidirectional relationships between sleep quality and daytime attention to pain remained significant even when controlling for pain intensity (Affleck, Urrows, Tennen, Higgins, & Abeles, 1996). These findings may also inform the relationship between sleep and mood. Attention to pain is not synonymous with mood, but the effects of both pain intensity and sleep quality on pain attention may be mediated by mood. The effect of other types of rheumatic disease symptoms on sleep has not been studied. Pain is certainly known to disrupt sleep in many populations (Morin, Kowatch, & Wade, 1989); however, given the range of symptoms in lupus it would also be worthwhile to investigate whether other symptoms affect sleep in lupus.

In the study of normal volunteers cited above (Totterdell et al., 1994), ratings on a general physical symptoms factor (back pain, body aches, eyestrain, sick or nauseous, cold symptoms) predicted that night's longer sleep latency, later sleep onset and more nighttime awakenings, but not sleep quality ratings. In the reverse sequence, tonight's sleep latency and sleep onset time did not predict tomorrow's symptoms, but number of awakenings and perceived sleep quality did predict symptoms.

Disease activity, symptoms and functional disability may all predict depressive symptoms in RA over somewhat long periods of time (Newman, Fitzpatrick, Lamb, & Shipley, 1989; Wolfe & Hawley, 1993). One study addressed the daily symptoms—mood link in RA (Affleck et al., 1992). In within-subjects analyses involving 75 days' ratings, pain and mood on the same day were related, but this relationship was only significant for 40.7% of participants (n=55). Higher overall RA disease activity predicted a stronger association between daily pain and mood.

Daily fatigue, sleep and mood in lupus. The descriptive data reported in chapter 3 further support the relevance of testing this model with daily data. Among women with lupus fatigue is consistently higher during the day than for a matched group of women who do not have lupus. Fatigue is not stable, however. It fluctuates cyclically day-to-day. Daily patterns in sleep and mood among these women suggest these variables may be related to fatigue. In the lupus group average total sleep time and the pattern of sleep day to day is similar to the comparison group. Total time spent in bed, which includes bed rest time before going to sleep and after awakening in the morning, is consistently higher in the lupus group. Further, the women increase substantially both time in bed and total sleep time on weekends. These strategies do not seem to alleviate fatigue, however. Fatigue tends to decrease on weekends but not as dramatically as the increased sleep and time in bed might suggest. On the contrary, sleep quality is poorer among the lupus group. Sleep efficiency, the ratio of total sleep time to time spent in bed, is an overall index of sleep quality. It is reduced among the lupus group, partially due to their consistently longer sleep latencies and wake time during the night. Based on clinical research on insomnia the lupus group's spending extra time in bed may be fostering their sleep initiation and maintenance difficulties, but this habit is not solely responsible for their sleep problems. Daily patterns in these sleep disruption indices are less cyclical than time in bed and total sleep time, suggesting that factors other than the women's efforts to sleep are driving the disruption. Lupus symptoms may be one factor affecting the sleep disruption. The daily patterns of sleep efficiency and fatigue do not clearly suggest a relationship between them; nevertheless, the degree of reduced sleep quality and increased daytime fatigue among the women implies a link. Depressed mood is not statistically different among the women with lupus, but mood does fluctuate cyclically. Although not significant, there is a tendency for mood to be more positive on weekends, suggesting a link to sleep and fatigue.

In summary, recent research provides some evidence that lupus symptoms, sleep quality, depressed mood and fatigue may be related on a daily basis; however, the causal interrelationships among these variables have not been widely studied in lupus or other rheumatic disease groups. The proposed fatigue model is tested here utilizing prospective, daily data from the study reported in chapter 3.

Method

Participants

Daily diary data from thirty-three women with SLE were used to test the proposed fatigue model. Chapter 3 contains a detailed description of these participants' recruitment for the study and their demographic profile. At the time of the study all these women were experiencing relatively mild disease activity. Rheumatologists for thirty-two of the women completed the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), a measure of current disease activity (Bombardier et al., 1992). Average SLEDAI scores ($M = 5.56$, $SD = 5.65$) were similar to those reported in a recent descriptive study comparing current disease activity and cumulative organ damage due to lupus ($M = 4.1$, $SD = 5.3$) (Hanly, 1996). This group tended to have milder disease activity than the 574 patient profiles reported in the SLEDAI validation study, however (Bombardier et al., 1992). All thirty-two women scored ≤ 20 on the SLEDAI, whereas in the validation study only 80.7% scored within that range, with the remaining 19.3% scoring between 20 and 45.Both the participants and their physicians marked two 100 mm visual analog scales on a scale from 0 to 100. The two ratings assessed current disease activity (from "none" to "most") and overall lupus case severity (from "least severe" to "most severe" case). The women rated current disease activity slightly higher than their physicians (means: participants = 37.53; doctors = 26.28; $t(31) = 2.55$, $p = .02$). Some of this discrepancy may be due to the time lag (generally one month or less) between when the participants and doctors completed these ratings. Participants and their doctors judged the overall severity of their case of lupus similarly (means: participants = 36.03; doctors = 39.69; $t(31) = -0.78$, ns).

Measures

Measures of fatigue, lupus disease activity, sleep quality, and depressive mood were collected prospectively through a daily diary format.

Daily fatigue. Twice daily participants rated a single 100 mm visual analog scale (VAS). The question, "To what degree are you experiencing fatigue right now?" was rated from 0 (no fatigue) to 100 (a great deal of fatigue). This item was intended as an overall index of current fatigue.

Daily sleep quality. A standard sleep log format was used to assess daily sleep patterns. Each morning participants described last night's sleep with several variables. Standard nightly sleep parameters derived from these reports included: total sleep time (TST), total time spent in bed (TIBTOT), total time in bed trying to sleep (TIBSLP), sleep latency (SLAT), wake time during the night after sleep onset (WASO), sleep efficiency percentage based on time trying to sleep (SE_SLP%), and sleep efficiency percentage based on total time in bed (SE_TIB%). Calculation of these measures is further elaborated in Chapter 3.

To test the fatigue model I wanted an overall index of sleep quality. Sleep efficiency, the ratio of total sleep time to time in bed, is commonly used as such an index. While the SE_SLP% variable is a more standard measure in sleep research, I was also interested in the effect on fatigue of additional time spent in bed by the women with lupus. The SE_TIB% measure includes bed rest before trying to sleep and again after waking in the morning; therefore, SE_TIB% was the measure of sleep quality used in all analyses reported here.

Daily mood. Twice daily, participants rated their mood with the Positive and Negative Affect Schedule (PANAS) (Watson et al., 1988). The PANAS consists of two 10-item mood adjective lists (Appendix E2). Participants rate whether each adjective has described their feelings within a specified time period on a five-point scale from "very slightly or not at all" to "extremely". Possible scores range from 10 to 50 on each scale. These scales assess two primary mood dimensions, positive affect (PA) and negative affect (NA) (Watson & Tellegen, 1985) . Because the two dimensions show consistently low intercorrelation in factor analytic studies (r = -.12 to -.23) and from validation studies in both normal and clinical populations, PA and NA are conceptualized as independent, bipolar factors (Kendall & Watson, 1989). NA contains components of both anxious (e.g., afraid, nervous, worried) and depressed (e.g., sad, lonely, blue) states. Low PA, conversely, more purely reflects depressed affect. Because the interest for this paper was in depressed affect, only the PA scores were used in analyses. Various investigators find low PA associated with fatigue-related states including cognitive and physical sluggishness, decreased concentration, and sleepiness (Thayer, 1989; Watson & Kendall, 1989).

Weekly lupus symptoms. Weekly throughout the diary participants completed a lupus symptoms checklist. A list of thirty-three common lupus symptoms was assembled with the help of Dr. Stephen Paget, a rheumatologist. He grouped the symptoms into six categories, based generally on the organ system involved. Participants rated the presence and severity of each symptom for the past week on a seven-point scale ranging from not present to severe (0 to 6) (Appendix F1).

Rather than summing symptoms ratings across all thirty-three symptoms, or summing scores within each organ system grouping, an exploratory factor analysis with oblique rotation was performed on the symptoms ratings at each time point. This analysis was used to identify symptom clusters that are more ecologically and psychometrically meaningful. Grouping the symptoms by organ system may be a useful heuristic in designing a questionnaire format or making certain treatment decisions, but it may not well represent women's everyday experience. Because lupus is a multisystem disease, individuals may tend to experience symptoms simultaneously from different organ systems. If so, these clusters are more likely relevant for daily sleep, mood and fatigue. Drawing on the original six categories suggested by Dr. Paget, the factor analysis solution was constrained to six factors to keep the results somewhat uniform across the three time points. Because of weak or split factor loadings, or non-occurrence among the women, seven items were omitted from the final six factors: menstrual changes, hair loss, high blood pressure, fever, urinary symptoms, swollen glands, and seizure (no occurrences). The resulting six symptom scales, their component items, and the Cronbach's alpha reliabilities across time are listed in Appendix F2.

Generally the factor structure conformed to Dr. Paget's symptom groups; however, there were symptoms that grouped differently than in the original list. The labels assigned to these factors were: pain symptoms, gastrointestinal symptoms, chest symptoms (lung and heart), skin symptoms, neurologic symptoms, and psychologic symptoms. The clusters seem to represent not only different organ system involvement, but also different levels of disease activity severity. For instance, skin symptoms may be very distressing and bothersome, but they are never life threatening. Chest and gastrointestinal symptoms such as abdominal pain and difficulty breathing, on the other hand, may indicate more severe problems such as peritonitis and pneumonia.

The pain symptoms cluster was chosen as the measure of disease activity for testing the fatigue model. This cluster includes five items rating the severity of joint pain, joint inflammation, joint stiffness, muscle pain or weakness; and headache. Summed severity ratings on these five items were used in all analyses reported here. Reliability coefficients for the pain symptoms scale on Nights 1, 7 and 14 of the diary were high (α = 0.89; 0.91; 0.93). The pain symptoms cluster was chosen for several reasons. First, along with fatigue, pain associated with arthritis, arthralgias, muscle pain and headaches is one of the most frequent, prevalent lupus symptoms (Hahn, 1997; Lahita, 1997; Schur, 1993). As noted in the literature review, pain has been the only symptom studied in relationship to fatigue, sleep or mood among other rheumatic disease groups (Affleck et al., 1992; Crosby, 1988; Crosby, 1991; Nicassio & Wallston, 1992; Stone et al., 1997). Using the pain cluster increases the ability of this study's findings to extend prior research findings. The pain, gastrointestinal, and psychological symptoms were more consistently strongly correlated ($r \geq .40$) with daily fatigue than the other symptom clusters. Psychological symptoms were eliminated from consideration because they are too confounded with mood. Pain symptoms seemed more likely than gastrointestinal symptoms to disrupt sleep (Morin et al., 1989) and affect daytime mood. In bivariate correlations these two clusters were somewhat differentially associated with the various daily sleep measures. The pain cluster was more strongly associated over the fourteen days with sleep efficiency, an overall index of sleep quality, and with positive affect.

One important question in constructing a model of fatigue is whether different types of symptoms are associated differentially with daily fatigue, sleep and mood. If so, their role as a direct or mediating mechanism in causing fatigue may also vary. There are sound theoretical arguments to suggest that the model represented in Figure 1 is not the only causal configuration among these variables, nor is it proposed as a comprehensive model of the fatigue experience. It would be worthwhile for theory development to explore the impact of various clusters of lupus symptoms on fatigue, as well as on mood and sleep. The purpose of this paper, however, is to test as adequately as possible the specific fatigue model proposed. The main justification for this constraint is to focus on fatigue as a troublesome clinical outcome and the potential intervention strategies made available if sleep and mood contribute to fatigue. The analyses presented here were limited to that goal. As a result, the pain symptoms cluster was chosen most likely to impact sleep, mood, and fatigue. This choice does not preclude the importance of exploring the impact of other symptoms clusters, or overall lupus disease activity on fatigue in the future.

Procedure

Participants in the study completed a baseline questionnaire followed by a daily structured diary for fourteen days. Women who returned a signed consent form were mailed the baseline questionnaire. This packet contained questions to screen for study eligibility and demographic information. After returning the baseline survey, women who met eligibility criteria were contacted by phone to schedule a convenient date to begin the daily diary. The diary was scheduled to begin as soon as possible after each woman had an appointment with her rheumatologist. In most cases the diary began within a month after a physician visit. For that targeted appointment date, the rheumatologist was asked to complete an ARA lupus diagnostic criteria checklist to verify SLE diagnosis (Tan et al., 1982) and the SLEDAI disease activity measure. For both groups an attempt was made to schedule the diary when the women would not be traveling away from home.

Daily diary protocols require dedication and consistency from participants. In order to engage these women in the process of keeping the diaries, a researcher was paired with each woman upon enrollment, maintained contact with her and kept track of her progress through the protocol. Researchers involved in the study were the investigator and three advanced undergraduate psychology students working as research assistants. On or before each woman's diary start date, a researcher met in person with her. This meeting was meant to establish rapport and familiarize her with the protocol. By explaining specifically what type of information the diary questions addressed, we encouraged the women to be trained observers actively involved in this process. This personalized interaction was also intended to minimize missing data. For example, the sleep log section asked for very specific variables regarding sleep schedules. Women were asked the time each night when they physically got into bed and the time they began trying to fall asleep. We asked them to distinguish between two activities they might not otherwise have considered distinct. We clarified that the times they recorded for these variables might sometimes be the same (e.g., you turn off the lights and try to sleep immediately upon getting into bed) and other times differ (e.g., you get into bed and read for 30 min before turning out the light). The women were encouraged to ask questions both at this meeting and throughout the diary, and were provided with phone numbers to contact both the researcher working with them and the investigator.

Everyone began the diary on a Thursday morning with a practice run-through of the daily diary protocol. Data from this practice day were not analyzed. Officially the diary began Thursday night (night 1). On each Thursday night (nights 1, 7, and 14) participants completed a written questionnaire containing the lupus symptoms severity measure. From Friday morning (day 1) through the second Thursday (day 14) participants completed a fourteen-day telephone call-in procedure. This procedure is a modified version of one used successfully at the City College of New York Sleep Disorders Center (Spielman, Saskin, & Thorpy, 1987). Soon after getting out of bed each morning, participants filled in information in a booklet, with each day's report designed as a script in first-person voice. Each morning's script included last night's sleep log and information not analyzed for this paper, including: past 24 hours' lupus and non-lupus health symptoms; caffeine and alcohol intake; and exercise (example diary page in Appendix D). Participants then called a voice-mail answering system and read the scripted diary report. The women were also encouraged to leave any procedural or other questions on the answering machine with their diary report. Each woman's researcher retrieved daily her call-in data and placed a reminder call to her that same day if she had forgotten to leave a report. The researchers also called participants during the diary to maintain rapport and answer questions as needed.

The daily fatigue VAS and PANAS were completed in written questionnaires. Based on baseline data, the typical midpoint of each woman's waking day was calculated. The women were asked to complete the fatigue and mood ratings at that midpoint time, usually in mid-afternoon, and again just before getting into bed. These times assessed mood for the first and second halves of a woman's day and fatigue, as the outcome, at the midpoint and end of her day.

Participants received $5 with the baseline questionnaire and another $35 after completing the diary. The money was offered to thank participants for their help and cover any telephone charges they may have incurred to complete the daily call-in reports.

Results

There are a number of different ways in which the proposed fatigue model could be evaluated. Under ideal circumstances, a set of linear equations involving both observed and latent variables could be developed to model the daily data as repeated measures and their associated error structures. This approach would provide an integrated assessment of the mediating roles that sleep and mood play between disease activity and fatigue, as well as the hypothesized reciprocal relationship between sleep and mood. Unfortunately, the small sample size and relatively small number of observations precluded use of a simultaneous equation technique.

One of the central components of the proposed fatigue model, the mediational hypothesis, can be evaluated directly using a repeated measures analysis of variance (RANOVA). This approach preserved the prospective relationships among the weekly and daily variables as opposed to collapsing them into summary means. As noted in Chapter 2 the reciprocality hypothesis can only be tested directly using a simultaneous equations approach. Testing the sleep—>mood and mood—>sleep effect (A1 and B1 in Fig. 1) in separate analyses fails to account for shared variance between the two directional paths, leading potentially to spurious results. In this study the sleep and mood reciprocality hypothesis was tested in two ways. First, each path was tested separately with a RANOVA model. Using separate models to test each directional path provides suggestive but not conclusive results. Second, the two reciprocal paths were analyzed simultaneously using a system of linear equations. As noted above, however, this approach limited interpreting the reciprocal relationship in the context of the full model, i.e., whether sleep and depression mediate between lupus symptoms and fatigue. Nevertheless, using both techniques to test the reciprocality hypothesis provided redundancy. Looking across both sets of findings aided in interpreting the reciprocality part of the model.

Procedure 5V in the BMDP statistical software package was used to test the RANOVA models (Dixon, 1992; Dixon & Merdian, 1992). The features of 5V are described in more detail in Chapter 3. In testing each path of the model, I fit the data against all four standardized covariance matrix structures provided in Procedure 5V: compound symmetry, autoregressive, banded autoregressive, and unstructured. Choosing the best fitting structure, especially with such complex models, is not a precise exercise. At the statistical level, one generally uses the log maximum likelihood (ML) estimator and/or Aikaike's Information Criterion (AIC) (Akaike, 1974) to judge model fit to the observed covariance matrix. Both statistics indicate a better model fit as their values approach zero. The AIC changes as a function of the number of degrees of freedom in the particular model being tested, thus, the measure penalizes the choice of a more complex model compared to models that are less complex. Akaike recommended the selection of the model that yields the smallest AIC value. McDonald & Marsh (McDonald & Marsh, 1990) have raised questions about this criterion as far as model selection is concerned, although Bozdogan (Bozdogan, 1987) is more positively disposed toward the measure.

In the present study, the choice of the appropriate error covariance matrix was guided by the constructs and models being studied, the data themselves, as well as statistical criteria. Daily trends in symptoms, sleep, mood and fatigue have begun to be described in other rheumatic disease groups but not in lupus (Affleck et al., 1992; Affleck et al., 1996; Stone et al., 1997). In Chapter 3 daily fatigue, mood and some sleep variables exhibited banded autoregressive covariance matrix structures, suggesting cyclic day-to-day trends in these variables. Whether a banded structure continues to emerge in exploring causal relationships between these variables and lupus symptoms is uncertain given the lack of precedent in the literature. The judgment process used to choose the best fitting structure was first to look at the AIC then at the ML values. Generally the structure with the lowest AIC was chosen; however, in several cases the lowest AIC and ML values were associated with two different matrix structures, creating ambiguity about the better-fitting matrix. In a small number of these situations, model results differed under the two matrix structures.

In addition to using the RANOVA to test for reciprocality, exploratory use was made of a multiple equation system for the same purpose. The SAS program PROC SYSLIN was the procedure used (SAS, 1996). This program allows the user to estimate the parameters of a multiple equation system using either a Limited Information Maximum Likelihood (LIML) or Full Information Maximum Likelihood (FIML) approach. Given the exploratory nature of this analysis, the procedure with the fewest assumptions regarding the data was chosen, the LIML approach.

Mediation and reciprocality using a repeated measures ANOVA approach

Figures 2 and 3 illustrate the analytic steps involved in testing this model. These mirror conceptually the steps described in Chapter 2 to test the model using cross-sectional data. The first step in testing mediation is to confirm *direct effects* among the predictor, mediator and outcome variables (Baron & Kenny, 1986). As shown in Figure 2, pain symptoms, the predictor variable, should significantly affect both the mediators sleep efficiency (path A) and mood (path B), as well as the outcome fatigue (path E). Both mediators, in turn, should affect the outcome. Sleep efficiency should affect fatigue (path C), and mood should affect fatigue (path D).

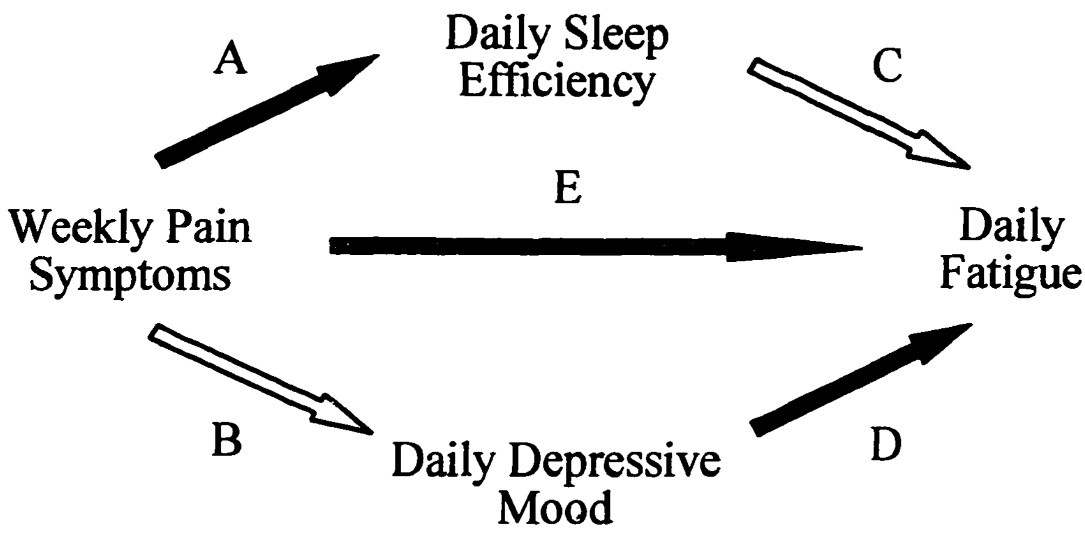

Figure 2. Direct effects on fatigue. This is the first step in testing the mediational model.

The second step, *mediation* involves testing simultaneously the effects of pain symptoms, sleep efficiency and mood on fatigue in one model. Sleep efficiency and mood are confirmed as mediators if their effects remain significant while pain symptoms' effect is reduced to nonsignificance (Baron & Kenny, 1986). An added dimension in this study compared to the cross-sectional analyses in Chapter 2 is the chronological relationship among the variables. Utilizing the prospective repeated measures for both sleep and mood, I tested the mediation model with two different chronological sequences. Figure 3 illustrates the two sequences with one daily cycle out of the fourteen days included in the repeated measures analyses. In path A–A1–D, sleep tonight predicts mood tomorrow afternoon; in path B–B1–C, mood today predicts sleep tonight. These analyses are represented by the following equations.

Path	Equation
A–A1–D:	Pain Symptoms + Sleep Efficiency + Positive Affect = Fatigue
B–B1–C:	Pain Symptoms + Positive Affect + Sleep Efficiency = Fatigue

Testing *reciprocal effects* between sleep efficiency and mood also involves analyzing mediation models using a RANOVA approach. Paths A1 and B1 in Figure 1 represent the proposed bidirectional effects between sleep and mood. As a preliminary step toward testing the full mediation models described above, these effects were tested with paths A–A1 and B–B1 to determine if sleep and mood mediate the effects of pain symptoms on each other. These analyses required using the same two chronological sequences as in the full models and are represented with the equations below:

Path	Equation
A–A1:	Pain Symptoms + Sleep Efficiency = Positive Affect
B–B1:	Pain Symptoms + Positive Affect = Sleep Efficiency

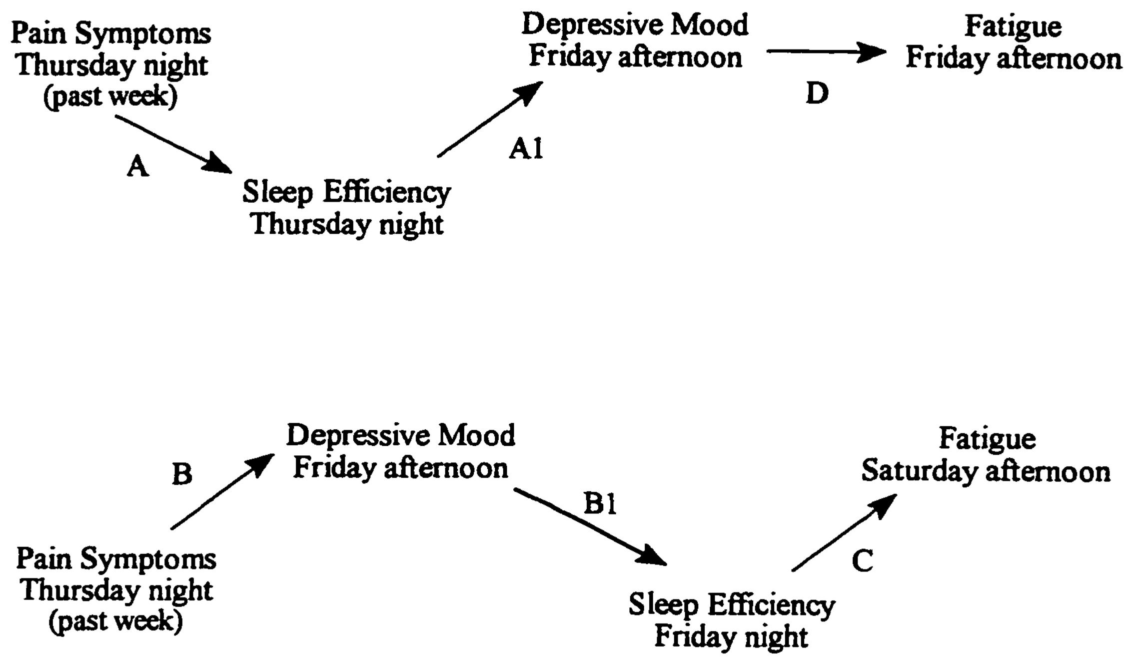

Figure 3. Mediation effects in two chronological sequences.

Direct effects. Using BMDP 5V the five paths shown in Figure 2 were tested with a repeated measures design using fourteen observations of the outcome variable and a single time varying covariate as the predictor variable. In all analyses the fatigue variable comprised the midday fatigue ratings for fourteen days. Because between groups analyses in Chapter 3 suggest midday fatigue is more salient than bedtime fatigue among the women with lupus, only midday fatigue was used to test the model. For the predictor variables, pain symptoms were assessed weekly; sleep efficiency and mood were assessed daily. The midday PA ratings were used as the mood variable to predict concurrent midday fatigue. Night 1 pain symptoms were used to predict sleep, mood and fatigue on days 1 through 7. Night 7 pain symptoms were used to predict sleep, mood and fatigue on days 8 through 14.

For example, for path A, daily sleep efficiency was the outcome variable with fourteen observations. Weekly pain symptoms were specified as a time varying covariate to test the effect of night 1 pain (Thurs.) on nights 1 through 7 of sleep efficiency (Thurs. through Weds.); and the effects of night 7 pain (second Thurs.) on nights 8 through 14 of sleep efficiency (second Thurs. through Weds). For path D, midday fatigue was the outcome with fourteen observations. Midday PA was matched day-by-day with fatigue as a time varying covariate.[1]

All five paths in Figure 2 were confirmed by a significant effect of the covariates on the respective outcomes. Paths A, C and D were best modeled by a banded

1 Attempt was made to test the model using both the midday and bedtime daily fatigue and PA variables. In the first stage of testing direct effects, Path B, in which symptoms predict mood, would not converge because of too much collinearity in the BMDP 5V analysis. This precluded using both midday and bedtime PA in further analysis.

autoregressive covariance matrix. The best fitting matrix was ambiguous for Paths B and E . For path E, a banded autoregressive structure fit best according to the AIC, and the effect of pain symptoms on fatigue was nonsignificant. An unstructured matrix fit best according to the ML, and the effect of pain symptoms on fatigue was significant. The ML values for these two matrix structures were compared and were not significantly different (there is no significance test for comparing AIC values); therefore, the results under the unstructured matrix were used to confirm the direct effect of pain symptoms on daytime fatigue. Choosing the unstructured matrix results was further justified by exploring the structure for daily fatigue alone, with no predictor variable. A one-way RANOVA on daytime fatigue for the fourteen days was performed. Here again the banded and unstructured matrices fit the fatigue data equally by statistical criteria.

For path B, a banded autoregressive structure fit best according to the AIC, and the effect of pain symptoms on daytime PA was nonsignificant. An unstructured matrix fit best according to the ML, and the effect of pain symptoms on daytime PA was significant. The ML values for these two matrix structures were found to be significantly different. To explore the structure of the PA data further, a one-way RANOVA on PA for the fourteen days was performed. The unstructured and banded matrices fit the data equally well, with no significant difference between them. Considering the nature of daily PA, the unstructured matrix is probably a better fit. This structure indicates more variable, unpatterned mood fluctuations day to day. There is no definite precedent for daily mood patterns in the literature. Mood tends to be more positive on weekends, but antecedent circumstances (e.g., stressful daily events) and individual differences can alter this pattern considerably (Thayer, 1989). In the results reported in chapter 3, daily patterns in PA were not very similar between women with lupus and women without lupus. There was a banded pattern overall in these data, but they did not exhibit a clear weekend–weekday trend, yet mood did fluctuate daily in both groups. While the results for path B are more ambiguous than the other direct effects, they seem to confirm that pain symptoms predict lower daytime positive affect.

Reciprocal effects. Results for the next analysis phase are summarized in Table 1. To investigate whether sleep efficiency and mood reciprocally affect each other, two models were analyzed. In path A–A1 (Fig. 1) daytime mood was the repeated measures outcome with fourteen observations. Pain symptoms and SE_TIB% were entered as time varying covariates which varied weekly and daily, respectively. In this design sleep each night predicts mood the next afternoon. In path B–B1 (Fig. 1) nightly SE_TIB% was the outcome, and pain symptoms and daytime PA were time varying covariates. In this design mood this afternoon predicts sleep tonight.

In path A–A1, SE_TIB% had a significant effect on PA, but pain symptoms did not, indicating that sleep efficiency mediated the effect of pain symptoms on daytime mood. A banded autoregressive structure best fit this model. In path B–B1, PA affected SE_TIB%, but pain symptoms also exhibited a marginally significant effect, thus PA was a somewhat weaker mediator of pain symptoms' impact on sleep efficiency.

Table 1. Reciprocal effects between sleep efficiency and positive affect.

Model [a]	Covariance Matrix	Max Log Likelihood	Akaike's (AIC)	Outcome	Predictor	beta [b]	Wald χ^2
Path A–A1	Banded autoregressive	-1562.37	-1576.37	Positive affect	Pain symptoms	-0.08	0.65
					Sleep efficiency	0.09	9.21 **
Path B–B1	Compound symmetry	-1599.46	-1601.46	Sleep efficiency	Pain symptoms	-0.19	2.38 †
					Positive affect	0.13	4.14 *

* $p < 0.05$ ** $p < 0.01$ † $p < 0.15$

[a] The paths correspond to those identified in Figure 3. They represent two chronological sequences in which the model was tested. See text for explanation.

[b] Unstandardized regression parameter estimates. These indicate the predicted amount of change in the outcome variable for each unit change in the predictor variable.

Mediation model. The full mediation model was tested with two chronological sequences. In both models pain symptoms, daily SE_TIB% and daytime PA were specified as time varying covariates to predict daytime fatigue as the outcome. The sequential relationships between sleep efficiency and positive affect were set up the same way as in the reciprocality analyses. The results are presented in Table 2.

In the first sequence, paths A–A1–D, both SE_TIB% and PA had significant effects on fatigue, but pain symptoms did not. These results indicate both last night's SE_TIB% and today's PA mediated the effects of weekly pain severity on today's fatigue. A banded autoregressive structure was chosen to best represent these results.

In the second sequence, paths B–B1–C, only SE_TIB% had a significant effect on fatigue. These results indicate that sleep efficiency tonight mediated both the effects of weekly pain severity and today's mood on tomorrow's fatigue. Contrary to results in the first sequence, mood did not mediate the effects of pain on fatigue; however, the mood measure was more chronologically distant from fatigue under this sequence. This sequence was best represented by a banded autoregressive structure.

Table 2. Mediational fatigue model: The effects of pain symptoms, sleep efficiency and daytime positive affect on daytime fatigue in two chronological sequences.

Model [a]	Covariance Matrix	Log Max Likelihood	Akaike's (AIC)	Predictor	beta [b]	Wald χ^2
Path A–A1–D	Banded autoregressive	-1994.00	-2008.00	Pain symptoms	0.13	0.22
				Sleep efficiency	-0.25	10.08 **
				Positive affect	-1.14	97.57 ***
Path B–B1–C	Banded autoregressive	-1883.09	-1896.09	Pain symptoms	0.15	0.22
				Positive affect	-0.06	0.21
				Sleep efficiency	-0.29	10.03 **

** $p < 0.01$ *** $p < 0.001$

[a] The paths correspond to those identified in Figure 3. They represent two chronological sequences in which the model was tested. See text for explanation.

[b] Unstandardized regression parameter estimates. These indicate the predicted amount of change in the outcome variable for each unit change in the predictor variable.

Reciprocality using a system of linear equations approach

As mentioned earlier, a more direct way to explore reciprocal causation between sleep and mood is by testing the effects simultaneously. Using a system of linear equations is one method of simultaneous analysis. The number of participants and observations in this study would not support testing the full fatigue model with this kind of analysis. There are enough observations to test only the reciprocality paths; however, the ratio of observations to number of equations was still quite low. As a result, this analysis was considerably more exploratory than the repeated measures approach. It was used to aid in interpreting the reciprocality part of the model.

Using the SYSLIN procedure in SAS, a system of twenty-seven equations was analyzed. Beginning with night 1 sleep, each night's SE_TIB% was used to predict the next day's PA, requiring fourteen equations. Using thirteen equations, each day's PA was used to predict that night's SE_TIB% (there was no PA measure available to predict the first night's sleep). In this system lower sleep efficiency significantly predicted lower positive affect the next day for eleven of the fourteen days. Lower positive affect significantly predicted lower sleep efficiency that night for eight days, and marginally ($p < .15$) predicted sleep for another two days.

One important consideration in any analysis of repeated measurements is the autocorrelated lagged effect of each measure on itself. Each day's mood might be expected to be a better predictor of tomorrow's mood than sleep, and the same would be expected of sleep affecting tomorrow night's sleep. To account for these lagged effects, the same system of equations was analyzed with the addition of a one-day lag. For example, when the outcome was sleep on Friday night, the predictors were mood on

Friday afternoon and sleep on Thursday night. In this system the first equation was the same as in the non-lagged analysis — night 1 sleep predicting day 1 mood. There was no prior mood measure to use as a lagged predictor for this first day.

Results for the remaining twenty-six equations that included lagged effects were as follows. On all days lagged sleep predicted the next night's sleep, and lagged mood predicted the next day's mood, both in positive directions. In the context of those autocorrelational effects, lower sleep efficiency significantly predicted lower positive affect for six of thirteen days. On one day lower sleep efficiency marginally ($p = 0.07$) predicted higher positive affect. Lower positive affect significantly predicted lower sleep efficiency that night for five days and marginally ($p < .15$) predicted sleep for another two days. The autocorrelated lagged effects were clearly stronger overall than the effects of the predictor variables; nevertheless, SE_TIB% and PA did continue to exert reciprocal effects on some days. Both these systems suggest that sleep efficiency had a stronger effect on mood than vice versa.

Discussion

The proposed fatigue model describes a process whereby fatigue may arise or be perpetuated through the interplay of several factors. The current study elaborates the model results reported in chapter 2. Analyzing this model within a daily time frame adds complexity to the results, but this complexity may be helpful for understanding fatigue and guiding further research and intervention efforts.

<u>Direct effects on fatigue, sleep and mood.</u> In independent analyses, weekly pain symptoms severity, reduced nightly sleep efficiency, and lower daily positive affect predict higher daily fatigue. The relationships of both sleep and mood with fatigue exhibited a

banded autoregressive pattern. This cyclic pattern suggests that the impact of sleep on daytime fatigue lasts as long as two days later; and that mood has an impact on concurrent fatigue and at least the next day's fatigue. The relationship of average weekly pain to daily fatigue is probably better described as more variable i.e., less cyclical than the effects of sleep and mood on fatigue, as demonstrated by the unstructured covariance matrix form. Pain symptoms also affect daily mood and sleep. Pain predicts lower positive mood; however, as explained in the results section, this conclusion is more tentative than the link between pain and fatigue. Weekly pain symptoms more clearly predict reduced daily sleep efficiency, and the effect follows a banded autoregressive cyclicity. There was ambiguity in choosing the better fitting covariance matrix for two analyses involving the pain symptoms variable — the effects of pain on both fatigue and mood. Part of this ambiguity may be due to methodology. Pain was assessed only at two weekly intervals, rather than daily. Having only two weekly pain assessments precludes detecting a cyclic pattern in pain.

Sleep and mood mediating daily fatigue. Two mediational pathways predicting fatigue were tested in the chronological sequences suggested in the model (Fig. 1). Sleep efficiency and positive affect both mediate the effects of pain symptoms severity on fatigue. Sleep and mood each emerge as a stronger mediator depending on their temporal proximity to fatigue. The severity of the past week's pain symptoms was assessed at the beginning of the first and second weeks of the study. Weekly pain severity has direct effects on the following seven days' sleep, mood and fatigue. The impact of pain on today's fatigue is mediated, however, by the effects of last night's sleep efficiency and today's mood (path A–A1–D in Table 2). In this sequence, mood concurrent with fatigue is the stronger mediator. In a different chronology, the impact of both pain and yesterday's mood on today's fatigue is mediated by last night's sleep efficiency (path B–B1–C in Table 2). In this sequence sleep occurs more proximally to fatigue than does mood, and its mediational effects on fatigue are stronger. Mood mediates the effects of pain only on the same day's fatigue; mood yesterday does not mediate pain's effect on today's fatigue.

The between groups results reveal that sleep latency and wake time during the night are both increased in the lupus group. Pain is likely reducing sleep efficiency through longer sleep latencies and sleep disruptions during the night (reported in chapter 3), resulting in unrefreshing sleep. Other rheumatic disease groups exhibit severe sleep fragmentation in sleep lab recordings. The degree of sleep disruption represented in these self-report data may be a low estimate of sleep fragmentation in the lupus group. Increased daytime fatigue is apparently one result of this ongoing sleep disruption.

Reciprocal effects between sleep and mood. The relationship between sleep quality and mood informs how these variables affect fatigue. The ability of sleep and mood to mediate the effects of pain symptoms on each other was examined with a repeated measures analysis approach. Decreased sleep efficiency tonight predicts lower positive mood tomorrow, more strongly than does increased pain. Sleep efficiency is, thus, likely one mechanism through which pain affects mood (path A–A1 in Fig. 1). Lower positive mood today also predicts lower sleep efficiency tonight. In this sequence, however, the effect of pain symptoms on sleep emerges as marginally significant (path B–B1 in Fig 1). This finding suggests that mood is a weaker mediator, and that pain and mood affect sleep quality somewhat independently. Pain may to some degree affect sleep efficiency through its impact on daytime mood, but pain also likely affects sleep directly or through other mechanisms. These findings suggest a degree of reciprocal effects between sleep and mood, with sleep quality affecting daytime mood more consistently than vice versa. One limitation in the findings for path B–B1 is that mood in the afternoon is somewhat distal to sleep, thus the relationship between them may be weaker. It would be useful to examine the effect of nighttime mood on sleep.

Using a system of linear equations, the results tend to support the first analysis. Reciprocal effects of today's mood on tonight's sleep, and tonight's sleep on tomorrow's mood occur on a number of days, even when controlling for autocorrelated lagged effects of the previous day. Sleep efficiency tends to affect mood more often than vice versa, but this is not a definite trend. While this analysis is quite exploratory, it suggests that bidirectional effects between sleep quality and mood do occur. The strength and consistency with which these effects occur over time can only be confirmed with a larger number of participants and observations.

How do the reciprocal effects inform the mediational effects? Potential pitfalls in microanalyzing the daily relationships among phenomena are a tendency toward linear thinking and an oversight of general trends. The mediational analysis results (Table 2) lend credence to particular causal sequences of events. The reciprocal effects between sleep and mood are reminders that these are not finite, linear processes. In these results sleep quality tends to emerge as a stronger mediator of fatigue, but mood in close temporal proximity also affects fatigue. Given the close conceptual link between positive affect and fatigue, current mood may be better understood as an essential component of fatigue. On an ongoing basis sleep and mood tend to affect each other, and this ongoing trend may compound their effect on fatigue. Pain symptoms contribute to this ongoing cycle. In these analyses, pain is the beginning or most distal event in the cycle, but that is an arbitrary position. All these phenomena — pain, sleep, mood and fatigue — fluctuate on an ongoing basis, as reported in chapter 3. There are probably other reciprocal causal influences among these variables in addition to the sleep—mood link. The overall value of these findings is to highlight the complex interrelationships among these phenomena, rather than promote a single, specific causal sequence.

Clinical implications. The fatigue model tested here is not purported to be a comprehensive model of fatigue etiology. Instead, it represents an attempt to define etiological pathways that offer potential intervention strategies, with an emphasis on possible nonpharmacological interventions. Existing interventions addressing sleep and mood disruptions may be ways to break the ongoing links among these processes. Anecdotally, people with lupus express concern with getting plenty of sleep to control fatigue and be able to function in various ways. These quotes from participants in two studies illustrate this sentiment:

> "Sometimes I feel fine and my day ends at midnight when I put down my magazine and turn out the light. Then there are days when I crawl into bed as soon as my kids are in bed and instantly fall asleep. I find that during times when I am the sickest I can handle things as long as I get lots of uninterrupted sleep. If I have to get up even once during the night my ability to cope with everything is reduced by half." (Ouellette, Bochnak, & McKinley, 1989)

> "I can't sleep properly. My work is not at its top level. I'm irritable and can't get things done at home. I always have the threat of joint pains if I get insufficient rest. I always need to limit late night activities and get a good night's sleep." (Knippen, 1988)

Paradoxically, too much attention to sleep, and trying too hard to get plenty of sleep may precipitate or perpetuate sleep disruption (Hauri & Fisher, 1986; Spielman & Glovinsky, 1997). The lupus group's tendency to spend extra time in bed, discussed in chapter 3, may reflect their concern with sleep and fatigue. For women experiencing sleep onset or maintenance problems, this habit may actually be counterproductive to feeling refreshed and rested (Spielman et al., 1987).

Much of the research linking sleep and depressive mood addresses only syndromal levels of depression. This study demonstrates that sleep quality is also related to more normal levels of mood fluctuations on an ongoing, daily basis. There has been almost no speculation that a link between mood and sleep disturbance at subclinical levels might be part of the same continuum as the sleep—depression relationship. Perhaps even minor sleep and mood disturbances, perpetuating each other over a long term, can contribute to the development of a more serious depressive episode, especially if another precipitating factor occurs. This body of research remains caught in a dilemma over cause versus effect (Moffaert, 1994). It is unclear whether the sleep anomalies or the depressive syndrome is the initial cause, and which phenomenon maintains the link. In diagnosing and treating insomnia, it is crucial to identify not only the conditions precipitating the insomnia, but also the predisposing and perpetuating conditions (Spielman & Glovinsky, 1997). The same approach would be helpful in disentangling the sleep–depression link.

For women with lupus, predisposing conditions for developing sleep or mood disturbance are probably not so different from those in the general population. For example, a tendency for heightened arousal during sleep or being a "night owl" (Horne & Ostberg, 1976) may predispose one for sleep maintenance or sleep onset difficulties, respectively (Spielman & Glovinsky, 1997). Genetic predisposition or certain cognitive styles (Clark & Beck, 1989) may predispose one to depressive disorders. In the general population, typical precipitating factors for sleep disturbance include situational factors like increased workload or deadlines, or having a new infant. Non-endogenous depression is usually precipitated by major stressful life events, often loss events like a loved one's death or a divorce. Over and above life's typical demands, however, having lupus brings a host of other challenges: symptoms, medications, disruptions in one's normal routine, worries about the disease and medical payments, etc. Any of these might precipitate sleep or mood disturbance.

Pain does reduce both daily sleep quality and positive mood, but whether pain precipitated the sleep disruptions and mood disturbance observed in this study cannot be determined. It is reasonable to suggest that pain has some effect in perpetuating these trends. Because lupus tends to have an unpredictable flare and remit course, over time symptoms may act as chronic precipitating or perpetuating stimuli for sleep and mood disturbance. The observed trend for sleep and mood disruptions to perpetuate each other may be sufficient for maintaining these disturbances even when lupus symptom severity is relatively low. Minor symptoms fluctuations and more severe flare episodes may create recurrent precipitating or perpetuating conditions that help maintain the sleep—mood link.

Limitations and future directions. In all analyses, all effects are relatively small, and do not explain a majority of the variance in fatigue. A larger sample and more observations over time would help with this problem. Another factor is that not all the women report levels of sleep efficiency or depressed mood to indicate cause for concern; therefore, pain symptoms do not affect sleep and mood for everyone. Only 3% report sleep efficiencies below 80%, while another 30% report sleep efficiencies below 90%. On the CESD depression measure 21.21% and 24.24% of the women, across three weekly measurements, score 16 or higher, which is the standard criterion used to indicate probable depressive disorder (Radloff, 1977). To increase analytic power and better determine the clinical relevance of this model, it would be useful to study subgroups of women. Groups might be selected based on more extreme fatigue or sleep disturbance.

Some of these effects, especially the impact of mood on sleep and fatigue, are relatively short-lived, perhaps because these phenomena exhibit diurnal fluctuations. It would be useful to test this model with multiple daily measures of mood and fatigue to see how their diurnal patterns may be parallel or divergent. Research has suggested that diurnal patterns in fatigue and pain differ (Stone et al., 1997). Such differential patterns likely inform how mood, fatigue and sleep are related. Similarly, daily pain fluctuation patterns over time vary within the RA population (Affleck, Tennen, Urrows, & Higgins, 1991). This finding suggests there may be identifiable subpopulations based on patterns of symptoms, sleep, mood or fatigue. If so, the best model of how these variables affect each other may also vary across these subgroups.

Only the effects of pain symptoms are explored here, but it would be worthwhile to test the effects of the other symptom clusters measured in this study. Further, the effects of non-pain symptoms were not controlled when testing the model. Using polysomnography, it would be useful to describe sleep in lupus compared to other rheumatic disease groups and to determine the relationship between sleep parameters and fatigue. In terms of mood, anxiety may be a useful construct for understanding the sleep—mood link. Too much attention to or worry about sleep may propagate insomnia. Anxious mood may be more relevant to that process than depressed mood. The findings for sleep anxiety in chapter 2 support this idea.

Conclusions. These results replicate and extend the fatigue model proposed in chapter 2. They indicate that fatigue can be affected by a variety of factors, including lupus symptoms, sleep quality and mood. These factors can be shown to affect fatigue independently, yet they are also interrelated over time. Modeling the interrelated processes among these factors may help understand chronic fatigue better and point to useful intervention strategies. These results also illustrate that a daily level of analysis can be useful in studying lupus fatigue and may, in fact, be necessary for understanding fatigue's complexity.

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APPENDICES

Appendix A

Participant Consent Forms

Lupus Group Consent Form

WDEH Project -- A 212-642-2513

Women's Daily Experiences and Health Project
DESCRIPTION OF PROJECT AND CONSENT FORM

Copy 1: Keep for Your Records

Purposes of the project:

You are being asked to participate in a research project about women with lupus. The aim of the project is to document the daily experiences of women with lupus and the ways these experiences affect how you feel each day. The responsible investigator is Paula S. McKinley, M.A. This project is being conducted under the auspices of both the Graduate Center of the City University of New York and the Cornell Arthritis Center at the Hospital for Special Surgery.

Project procedures:

If you agree to participate, you will be asked to fill out a Health History questionnaire about physical symptoms, sleep habits, medication and general information about yourself. One use of these questions will be to determine if you have certain serious medical or sleep problems. If you are eligible to participate you will be asked to keep a kind of diary about your daily experiences. Unlike a normal diary, however, you will be asked specific questions each day about your sleep, moods, fatigue and physical symptoms. For two weeks you will be asked to report sleep habits and physical symptoms by calling an answering machine soon after getting up each morning. You will receive a booklet containing specific questions. You will simply read your answers to the questions into the answering machine. This should take no longer than 5 minutes each day.

At two times each day, once in the afternoon and at bedtime, you will fill out a brief written questionnaire about how you have felt during the day. These two questionnaires take about 1 minute each. At the beginning, middle and end of the two week diary you will be asked to fill out another questionnaire about experiences during the past week, requiring about 20 minutes. Finally, you will be asked to provide the names of between two and five casual friends who are generally like you but do not have lupus. One or more of these friends will be contacted and asked to participate in this project. These women will answer the same questions as you except there will be no mention of lupus, and they will not be told who gave their name to preserve your confidentiality.

When you begin participating in the project, your lupus physician will also be asked to fill out a questionnaire about your lupus symptoms. Ideally, we will arrange for you to begin the two-week diary the same day or soon after an appointment with your rheumatologist so he or she can answer questions about your current lupus symptoms.

When you receive the first questionnaire (Health History), you will receive $5.00 to thank you for completing the questionnaire. When you complete the two week diary, you will receive another $35.00 in appreciation for your participation. You will receive these monetary "thank yous" even if none of the friends you refer to the project agrees to participate. When you begin the project, the researcher will offer to loan you a portable alarm clock or watch to use. You may find the clock helpful in remembering when to fill out the daily questionnaires. If you borrow a clock, you will be expected to return it before receiving the $35.00. You will receive a postage paid envelope in which to return the clock.

Risks:

Participating in this project should pose no risks to you. If you feel distress in response to any of the activities you may choose not to complete that part of the project. Should the project raise a more general sense of discomfort, you may call Paula McKinley, M.A., the Principal Investigator, at 212-642-2513. You may choose not to participate, and you may withdraw from the project at any time. Your participation or lack of participation will in no way affect the extent or quality of care you may be receiving from the Hospital for Special Surgery (HSS) or from physicians, health care and support services affiliated with the hospital.

Benefits:

The benefits of participating will be two-fold. First, after you have completed all parts of the project, the researcher will conduct a review session with you in person or by phone. We will review the daily patterns of sleep you reported and offer suggestions about how you may be able to change some of your habits to feel and function better during the day. This session is not meant to be a treatment of any kind but may prove to be helpful to you. In this session you will also be asked if you have concerns about your sleep or daily functioning. If so, you will be offered the names of appropriate experts in sleep disorders, medicine or psychology from whom you may seek treatment if you choose. Second, on a larger scale the project should help us understand the effects of different sleep habits and patterns, moods, fatigue and physical symptoms on daily life among women with lupus. This information will be used to formulate methods of treatment and of educating health care providers about this area in the future.

Confidentiality:

All information from each participant will be kept confidential and will be kept in a locked file cabinet at the Graduate Center of CUNY. All sleep diaries and questionnaires from each participant will be identified only by randomly assigned code numbers.

How to find out more:

If you have any questions or feel concerned about any part of the project while participating, you may call Paula S. McKinley, MA, the responsible investigator at 212-642-2513. If necessary to properly address your concerns, she may refer you to one of the consultants for the study, one of whom is a physician and the other an expert in sleep disorders. Questions also may be directed to the Graduate Center Office of Sponsored Research at 212-642-2061.

CONSENT TO PARTICIPATE:

I have read the description of the project. I understand that my participation is voluntary and that I am free to withdraw consent and discontinue participation at any time. I understand that, based on information provided by me, I may not be eligible to participate. I understand the activities in which I am being asked to participate and that I am agreeing for my lupus physician to provide information about my symptoms. I also understand that my confidentiality will be maintained. I agree to participate.

Date: ______________

Participant's Name: (please print)

____

Signature:_________________________

PLEASE SIGN AND KEEP THIS FORM FOR YOUR RECORDS

Please sign Copy 2 and return to the researcher.

Comparison Group Consent Form

WDEH Project -- B 212-642-2513

Women's Daily Experiences and Health Project
DESCRIPTION OF PROJECT AND CONSENT FORM

Copy 1: Keep for Your Records

Purposes of the project:

You are being asked to participate in a research project about women's daily health. The aim of the project is to document the daily experiences of women and the ways these experiences affect how you feel each day. The responsible researcher is Paula S. McKinley, M.A. This project is being conducted under the auspices of both the Graduate Center of the City University of New York and the Cornell Medical Center.

Project procedures:

If you agree to participate, you will be asked to fill out a Health History questionnaire about physical symptoms, sleep habits, medication and general information about yourself. One use of these questions will be to determine if you have certain serious medical or sleep problems. If you are eligible to participate you will be asked to keep a kind of diary about your daily experiences. Unlike a normal diary, however, you will be asked specific questions each day about your sleep, moods, fatigue and physical symptoms. For two weeks you will be asked to report sleep habits and physical symptoms by calling an answering machine soon after getting up each morning. You will receive a booklet containing specific questions. You will simply read your answers to the questions into the answering machine. This should take no longer than 5 minutes each day.

At two times each day, once in the afternoon and at bedtime, you will fill out a brief written questionnaire about how you have felt during the day. These two questionnaires take about 1 minute each. At the beginning, middle and end of the two week diary you will be asked to fill out another questionnaire about experiences during the past week, requiring about 20 minutes. Finally, you will be asked to provide the names of between two and five casual friends who are generally like you. One or more of these friends will be contacted and asked to participate in this project. These women will not be told who gave their name to preserve your confidentiality.

When you receive the first questionnaire (Health History), you will receive $5.00 to thank you for completing the questionnaire. When you complete the two week diary, you will receive another $35.00 in appreciation for your participation. You will receive these monetary "thank yous" even if none of the friends you refer to the project agrees to participate. When you begin the project, the researcher will offer to loan you a portable alarm watch or clock to use. You may find the watch helpful in remembering when to fill out the daily questionnaires. If you borrow a watch, you will be expected to return it before receiving the $35.00. You will receive a postage paid envelope in which to return the watch.

Risks:

Participating in this project should pose no risks to you. If you feel distress in response to any of the activities you may choose not to complete that part of the project. Should the project raise a more general sense of discomfort, you may call Paula McKinley, M.A., the Principal Investigator, at 212-642-2513. You may choose not to participate, and you may withdraw from the project at any time. Your participation or lack of participation will in no way affect the extent or quality of care you may be receiving from the Cornell Medical Center or its affiliated hospitals.

Benefits:

The benefits of participating will be two-fold. First, after you have completed all parts of the project, the researcher will conduct a review session with you in person or by phone. We will review the daily patterns of sleep you reported and offer suggestions about how you may be able to change some of your habits to feel and function better during the day. This session is not meant to be a treatment of any kind but may prove to be helpful to you. In this session you will also be asked if you have concerns about your sleep or daily functioning. If so, you will be offered the names of appropriate experts in sleep disorders, medicine or psychology from whom you may seek treatment if you choose. Second, on a larger scale the project should help us understand the effects of different sleep habits and patterns, moods, fatigue and physical symptoms on women's daily lives. This information will be used to formulate methods of treatment and of educating health care providers about this area in the future.

Confidentiality:

All information from each participant will be kept confidential and will be kept in a locked file cabinet at the Graduate Center of CUNY. All sleep diaries and questionnaires from each participant will be identified only by randomly assigned code numbers.

How to find out more:

If you have any questions or feel concerned about any part of the project while participating, you may call Paula S. McKinley, MA, the responsible investigator at 212-642-2513. If necessary to properly address your concerns, she may refer you to one of the consultants for the study, one of whom is a physician and the other an expert in sleep disorders. Questions also may be directed to the Graduate Center Office of Sponsored Research at 212-642-2061.

CONSENT TO PARTICIPATE:

I have read the description of the project. I understand that my participation is voluntary and that I am free to withdraw consent and discontinue participation at any time. I understand that, based on information provided by me, I may not be eligible to participate. I understand the activities in which I am being asked to participate. I also understand that my confidentiality will be maintained. I agree to participate.

Date: ______________

Participant's Name: (please print)

____

Signature:___________________________

PLEASE SIGN AND KEEP THIS FORM FOR YOUR RECORDS

Please sign Copy 2 and return to the researcher.

Appendix B
Daily Diary Protocol

The study reported in Chapters 3 and 4 involved a two-week daily diary protocol. This protocol is outlined below.

1. Practice Day: Thursday
   A practice run-through of Sleep Diary and Daily Questions. Participants were told this was practice, to become accustomed to the procedure. The researcher paired with each participant monitored her call-in data on this day to make sure she followed the protocol and answered all questions in the diary script correctly. A researcher then called each woman to correct any problems with the protocol and answer her questions before the first official diary report the next day. These practice data were excluded from analyses.

2. Night 1: Thursday night
   On the night of the Practice Day, participants completed the following questionnaires about one hour before bedtime:

   * Current Medications chart listing all prescription and non-prescription medications currently being taken
   * Piper Fatigue Scale
   * CESD depression scale
   * Lupus disease symptoms checklist — self-rated symptom severity during past week (Lupus Group only)

3. Days 1 - 14: Friday through the second Thursday

   * Call-in Sleep Diary in the morning after getting out of bed. Included reports of yesterday's activities, last night's sleep and lupus symptoms (Lupus Group only) and general physical illness symptoms (both groups) of past 24 hours.
   * Daily Questions at the midpoint of waking day and again at bedtime. Included fatigue VAS rating and PANAS mood scale.

4. Nights 7 and 14: Thursday nights
   On the nights of Days 7 and 14, in addition to the bedtime set of Daily Questions participants completed these measures:

   * Chart for reporting any changes in medications during the past week
   * Piper Fatigue Scale
   * CESD depression scale
   * Lupus disease symptoms checklist — self-rated symptom severity during past week (Lupus Group only)

5. Day 15:
   Participants made one final call-in report to confirm the times they completed the Day 14 Daily Questions and the Night 14 Questionnaire. The purpose of this call was simply to confirm their completion of the last day's activities.

Appendix C

Fatigue Measures

Appendix C1

The Piper Fatigue Scale

Note: This scale was modified from the original to assess fatigue "now" and fatigue for the "past 24 hours."

NIGHT 7: QUESTIONNAIRE Today's Day and Date:________________

Tonight, please fill out this questionnaire no earlier than 1 hour before you go to bed. The questionnaire takes about 20 to 30 minutes to complete. Tomorrow morning, please call in your sleep diary information as you have every day. The diary script for DAY 8 begins on the page following this questionnaire.

Some Questions About Fatigue

DIRECTIONS:
The following questions ask about some activity or feeling which may be related to fatigue as you experience it. For many of these questions you will be asked to place a vertical mark through a horizontal line. This vertical mark should be placed through the exact spot on the line which best indicates your rating of the question. This vertical mark may be placed <u>anywhere</u> along the horizontal line.

EXAMPLE #1:
For example, if going to music concerts is one of your favorite activities, you might answer the following question in this way:

To what degree do you like to go to concerts?

(example)

Not at all ___________________________________|_______ **A great deal**

EXAMPLE #2:
As another example, imagine that you only ate breakfast on Saturdays and Sundays because you are rushing out to work the other days of the week. If you were asked the following question your answer might look like this:

How frequently do you eat breakfast each week, including weekends?

(example)

Seldom ____|____ **Often**

If, however, you ate breakfast every day, you would make a mark all the way on the right end of the line.

1. What is the time RIGHT NOW? (Circle AM or PM) ____:____ AM PM

1a. To what degree are you experiencing fatigue now?

No fatigue ____ *A great deal of fatigue*
0 *10*

2. How severe is the fatigue which you are experiencing now?

No fatigue ____ *Worst fatigue experienced*
0 *10*

If you indicated in Questions 1 & 2 that you feel *no fatigue* now, please skip to Question 12. If you marked anything higher than 0 (No fatigue) in #1 and #2, please continue.

3. How long have you been feeling fatigued? (Check only one answer)

_____ *Minutes* _____ *Hours* _____ *Days* _____ *Weeks* _____ *Months*

_____ *Other, please describe:*____________________________________

4. During the period of time you have been feeling fatigued (the time you checked in Question #3), how would you describe the fatigue you have felt?

Continuous *(no breaks or relief from fatigue)* ____ Intermittent *(comes and goes)*

5. How would you describe the fatigue which you are feeling now?

Chronic *(has lasted more than one month)* ____ Acute *(has lasted less than one month)*

6. How would you describe the fatigue which you are feeling now?

Localized *(to a specific muscle, body part or area)* ____ Generalized *(whole body is fatigued)*

To what degree would you describe the fatigue you are experiencing now as:

7. *Unpleasant* ____ *Pleasant*
8. *Disagreeable* ____ *Agreeable*
9. *Protective* ____ *Destructive*
10. *Negative* ____ *Positive*
11. *Normal* ____ *Abnormal*

For the next section, rate how you feel RIGHT NOW, even if you are not feeling fatigued now.

Right now I feel. . .

12. *Refreshed*____ *Exhausted*
13. *Weak* ____ *Strong*
14. *Awake* ____ *Sleepy*
15. *Lively* ____ *Listless*
16. *Alert* ____ *Drowsy*
17. *Refreshed*____ *Tired*

Right now I feel. . . (Please make a mark on every line)

18. *Unenergetic*____________________ *Energetic*

19. *Sluggish*____________________ *Vigorous*

20. *Bored* ____________________ *Interested*

21. *Calm* ____________________ *Nervous*

22. *Impatient*____________________ *Patient*

23. *Motivated*____________________ *Unmotivated*

24. *Sad* ____________________ *Happy*

25. *Relaxed*____________________ *Tense*

26. *Depressed*____________________ *Exhilarated*

27. *Unable to concentrate*____________________ *Able to concentrate*

28. *Unable to remember*____________________ *Able to remember*

29. *Unable to think clearly*____________________ *Able to think clearly*

Please answer the next questions based on any fatigue you have felt in the PAST 24 HOURS.

30. To what degree did you experience fatigue in the past 24 hours?

    *No fatigue*____________________ *A great deal of fatigue*

31. How severe was the fatigue you experienced in the past 24 hours?

    *No fatigue*____________________ *Worst fatigue ever experienced*

32. How would you describe the **intensity** or **severity** of the fatigue you experienced in the past 24 hours?

    Mild ____________________*Severe*

33. When you felt fatigued in the past 24 hours, how long did it last ? (Check only one answer)

    _____ *Minutes* _____ *Hours* _____ *Days* _____ *Weeks* _____ *Months*

    _____ *Other, please describe:*____________________

34. How would you describe the fatigue you felt in the past 24 hours?

    Continuous *(no breaks or relief from fatigue)*____________________ Intermittent *(comes and goes)*

35. How would you describe the fatigue you felt in the past 24 hours?

    Chronic *(lasted more than one month)* ____________________ Acute *(lasted less than one month)*

36. How would you describe the fatigue you felt in the past 24 hours?

    Localized *(to a specific muscle, body part or area)*____________________ Generalized *(whole body is fatigued)*

To what degree would you describe the fatigue you experienced in the PAST 24 HOURS as:

37. *Unpleasant*____ *Pleasant*

38. *Disagreeable*____ *Agreeable*

39. *Protective*____ *Destructive*

40. *Negative*____ *Positive*

41. *Normal* ____ *Abnormal*

42. To what degree has your fatigue changed in the PAST WEEK?

____

Decreased *Same* *Increased*

For the next questions, please rate the degree of distress or interference you have experienced in your activities during the PAST 24 HOURS as a result of your fatigue. Place a vertical mark through each line at the exact spot which best indicates your rating.

In the Past 24 Hours:

43. To what degree has fatigue **caused you distress**?

*No distress*____ *A great deal of distress*

44. To what degree has fatigue you **interfered with your ability to clean your house/home**?

None ____ *A great deal*

45. To what degree has fatigue **interfered with your ability to cook for yourself**?

None ____ *A great deal*

46. To what degree has fatigue **interfered with your ability to bathe or wash yourself**?

None ____ *A great deal*

47. To what degree has fatigue **interfered with your ability to read**?

None ____ *A great deal*

48. To what degree has fatigue **interfered with your ability to dress yourself**?

None ____ *A great deal*

49. To what degree has fatigue **interfered with your ability to complete your work (paid work, <u>not</u> housework) or school activities**?

None ____ *A great deal*

50. To what degree has fatigue **interfered with visiting or socializing with friends**?

None ____ *A great deal*

51. To what degree has fatigue **interfered with your ability to engage in sexual activity**?

None ____ *A great deal*

52. To what degree has fatigue **interfered with your ability to engage in the kind of activities you enjoy doing**?

None ____ *A great deal*

Please tell us more about fatigue in your own words:

53. **Overall, what do you think is most directly contributing to or causing the fatigue you are experiencing NOW (or experienced in the PAST 24 HOURS)?**

54. **Overall, when you experienced fatigue in the past 24 hours, what was the best thing you found which relieved the fatigue?**

55. **Is there anything else that would describe your fatigue better to us?**

Appendix C2
Piper Fatigue Scale
Reliability Coefficients for New Subscales Derived from Factor Analyses

Revised Scale & Items	Piper's Original Subscale	Cronbach's Alpha Night 1	Night 7	Night 14
Temporal: To what degree are you experiencing fatigue now?	temporal	0.74	0.64	0.56
Fatigue now is: intermittent — continuous	temporal			
Fatigue now is: acute — chronic	temporal			
To what degree has fatigue changed in past week?	temporal			
Severity: How severe is fatigue now?	severity	0.98	0.94	0.90
How would you describe the intensity or severity of fatigue now?	severity			
Affective: Fatigue now is: pleasant — unpleasant	affective	0.81	0.86	0.90
Fatigue now is: agreeable — disagreeable	affective			
Fatigue now is: protective — destructive	affective			
Fatigue now is: positive —negative	affective			
Fatigue now is: normal — abnormal	affective			
Tiredness: Right now I feel: refreshed — exhausted	sensory	0.88	0.96	0.93
Right now I feel: strong — weak	sensory			
Right now I feel: lively — listless	sensory			
Right now I feel: refreshed — tired	sensory			
Right now I feel: energetic — unenergetic	sensory			
Sleepiness: Right now I feel: awake — sleepy	sensory	0.85	0.86	0.76
Right now I feel: alert — drowsy	sensory			
Anxiety: Right now I feel: calm — nervous	sensory	0.81	0.76	0.85
Right now I feel: patient — impatient	sensory			
Right now I feel: relaxed — tense	sensory			

Revised Scale & Items	Piper's Original Subscale	Cronbach's Alpha Night 1	Night 7	Night 14
Motivation:		0.44	0.68	0.69
Right now I feel: interested — bored	sensory			
Right now I feel: motivated — unmotivated	sensory			
Cognitive:		0.88	0.91	0.91
Right now I feel: able / unable to concentrate	sensory			
Right now I feel: able / unable to remember	sensory			
Right now I feel: able / unable to think clearly	sensory			
Fatigue consequences:		0.88	0.88	0.92
To what degree has fatigue . . .				
caused you distress	severity			
interfered with your ability to clean your house/home	severity			
interfered with your ability to cook for yourself	severity			
interfered with your ability to bathe or wash yourself	severity			
interfered with your ability to read	severity			
interfered with your ability to dress yourself	severity			
interfered with your ability to complete your work (not housework) or school activities	severity			
interfered with visiting or socializing with friends	severity			
interfered with your ability to engage in sexual activity	severity			
interfered with your ability to engage in the kind of activities you enjoy doing	severity			
Items omitted from scale				
Right now I feel: happy — sad	sensory			
Right now I feel: exhilarated — depressed	sensory			

Appendix C3
The Fatigue Severity Scale

The following statements refer to fatigue which you may experience from time to time and may be experiencing now. Circle one number to indicate how much you agree or disagree with each statement. Please base your answers on the way you have experienced fatigue in the ***past month***.

	Strongly Agree						Strongly Disagree
1. My motivation is lower when I am fatigued.	1	2	3	4	5	6	7
2. Exercise brings on fatigue.	1	2	3	4	5	6	7
3. I am easily fatigued.	1	2	3	4	5	6	7
4. Fatigue interferes with my physical functioning.	1	2	3	4	5	6	7
5. Fatigue causes frequent problems for me.	1	2	3	4	5	6	7
6. Fatigue prevents sustained physical functioning (stamina).	1	2	3	4	5	6	7
7. Fatigue interferes with carrying out certain duties and responsibilities.	1	2	3	4	5	6	7
8. Fatigue is one of the three most disabling symptoms I have.	1	2	3	4	5	6	7
9. Fatigue interferes with my work, family, or social life.	1	2	3	4	5	6	7

Appendix D

Daily Diary Script

DAY 7: Day and Date__________________ ID#______

When you GET OUT OF BED get the Daily Questions packet for today, and call 212-642-2531 to report this information to the answering machine.

ABOUT YOUR ACTIVITIES YESTERDAY________________:
Based on the past 24 hours, from the time you got up YESTERDAY until now.

1. Hello, this is _________(your name or project ID#).
2. Today is__________________(day of week & date).
3. Yesterday I dozed or took a nap ____times for a total of _____hours, _____minutes of sleep.
4. Caffeine only: I drank ____cups of coffee or tea, and ____ caffeinated soft drinks *(12 oz. can or equivalent).*
5. I drank ________servings of alcohol *(12 oz. beer OR 6 oz. wine OR drink with 1 1/2 oz. hard liquor).*
6. Yesterday I exercised by ______________________________*(types of exercise).* I got a total of _____hours, _____minutes of exercise.
7. Yesterday I answered the "Daily Questions" at these times:

Midday Questions time: __________ am/pm Bedtime Questions time: __________ am/pm

ABOUT LAST NIGHT'S SLEEP:
*(Note: You may get into bed to read, watch TV, etc. before you begin **trying** to fall asleep.)*

8. Last night I got into bed at ________(am/pm) and began trying to fall asleep at________(am/pm).
9. It took me _______hours, ______minutes to fall asleep.
10. During the night I woke up _____times and was awake a total of _____hours,____minutes.

(NOTE: If you woke up this morning then dozed or went back to sleep before getting up for the day, count that as one of your "during the night" wake-up times.)

11. The reasons I woke up during the night were:______________________________

(Briefly tell what awakened you--infant feeding time, pain, neighbor noise, alarm, etc.)

12. My WAKE-UP TIME this morning was _______am/pm *(last woke up and did not go back to sleep).*
13. I actually got out of bed at ________am/pm.
14. The total amount of sleep I got *(not counting the time you spent awake during the night, reported above)* was ________hours,________minutes.
15. My overall sleep quality last night was______ ***0 = Very good quality, restful or refreshing***
10 = Poor quality, restless or unrefreshing

Health Report: Past 24 Hours

Briefly describe any lupus-related symptoms you experienced in the PAST 24 HOURS.

16. My lupus symptoms in the past 24 hours were:_______________________________________

Please rate the overall severity of lupus symptoms (based on your experiences with lupus, not in comparison to other people with lupus) on a scale from 0=No symptoms to 10=Severe symptoms.

17. My rating of lupus symptoms in the past 24 hours is __________

Briefly, describe any illness or symptoms NOT related to lupus in the past 24 hours (Examples: cold, flu).

18. My non-lupus symptoms (or illness) in the past 24 hours were:_________________________

Rate your non-lupus symptoms on a scale from 0 = None to 10 = Severe symptoms, was ill

19. My rating of non-lupus symptoms in the past 24 hours is ___________

Please leave a phone number where you can be reached if you are going to be away from home.

Now, please get the *alarm watch* and *Daily Questions booklet*. Keep the booklet with you today, and fill it out at the times shown, both DURING THE DAY and TONIGHT AT BEDTIME.

TONIGHT, there is a Night 7 questionnaire to fill out no earlier than 1 hour before you go to bed; it takes about 20 minutes to complete. Tonight and Night 14 are the only remaining nights when you are asked to fill out these nighttime questionnaires.

You have finished half the project!
Hang in there, and thanks again for your help!

Appendix E

Depressive Symptoms and Mood Measures

Appendix E1
Center for Epidemiological Studies Depression Scale (CESD)

Please circle the number under the choice that best describes your feelings in the past week.

During the past week:		**Rarely** (less than 1 day)	**Some of the Time** (1-2 days)	**Occasionally** (3-4 days)	**Most of the Time** (5-7 days)
1.	I was bothered by things that don't usually bother me.	0	1	2	3
2.	I did not feel like eating; my appetite was poor.	0	1	2	3
3.	I felt that I could not shake off the blues even with help from my family or friends.	0	1	2	3
4.	I felt that I was just as good as other people.	0	1	2	3
5.	I had trouble keeping my mind on what I was doing.	0	1	2	3
6.	I felt depressed.	0	1	2	3
7.	I felt that everything I did was an effort.	0	1	2	3
8.	I felt hopeful about the future.	0	1	2	3
9.	I thought my life had been a failure.	0	1	2	3
10.	I felt fearful.	0	1	2	3
11.	My sleep was restless.	0	1	2	3
12.	I was happy.	0	1	2	3
13.	I talked less than usual.	0	1	2	3
14.	I felt lonely.	0	1	2	3
15.	People were unfriendly.	0	1	2	3
16.	I enjoyed life.	0	1	2	3
17.	I had crying spells.	0	1	2	3
18.	I felt sad.	0	1	2	3
19.	I felt that people disliked me.	0	1	2	3
20.	I could not get "going".	0	1	2	3

Appendix E2
The Positive and Negative Affect Schedule (PANAS)

The PANAS was completed at the midpoint and end of each participant's waking day. Both versions of the scale are shown. Positive affect items are noted with (PA). Negative affect items are noted with (NA).

Midpoint of waking day rating:

Overall, how have you felt since you woke up this morning?

Ratings: (write a rating for all words below)

1	2	3	4	5
Very Slightly or Not at All	A Little	Moderately	Quite a Bit	Extremely

interested	(PA)_	distressed	(NA)_	excited	(PA)_
upset	(NA)_	strong	(PA)_	guilty	(NA)_
scared	(NA)_	hostile	(NA)_	enthusiastic	(PA)_
proud	(PA)_	irritable	(NA)_	alert	(PA)_
ashamed	(NA)_	inspired	(PA)_	nervous	(NA)_
determined	(PA)_	attentive	(PA)_	jittery	(NA)_
active	(PA)_	afraid	(NA)_		

TIME RIGHT NOW? _________AM/PM

Tonight before you go to bed please complete the second set of Daily Questions on the other side of this page > > > > >

****

Bedtime Rating:

Overall, how have you felt since you answered these questions earlier today?

Ratings: (write a rating for all words below)

1	2	3	4	5
Very Slightly or Not at All	A Little	Moderately	Quite a Bit	Extremely

interested	(PA)_	distressed	(NA)_	excited	(PA)_
upset	(NA)_	strong	(PA)_	guilty	(NA)_
scared	(NA)_	hostile	(NA)_	enthusiastic	(PA)_
proud	(PA)_	irritable	(NA)_	alert	(PA)_
ashamed	(NA)_	inspired	(PA)_	nervous	(NA)_
determined	(PA)_	attentive	(PA)_	jittery	(NA)_
active	(PA)_	afraid	(NA)_		

TIME RIGHT NOW? _________AM/PM

Appendix F

Lupus Symptoms Measure

Appendix F1
Weekly Lupus Symptoms Checklist: Original Items

Please rate your lupus symptoms during the PAST WEEK. For each symptom, write a rating from 0 to 6 that best describes the ***worst*** *or* ***highest*** *each symptom has been in the past week.*

RATINGS:	0	1	2	3	4	5	6
	Not present in past month			Moderate			Severe

Part A

headache	____	depression	____
mood swings	____	numbness, tingling, weakness or paralysis of arms or legs	____
memory loss, problems with thinking	____	vision problems or abnormalities	____
anxiety	____	seizure (convulsion)	____

Part B

sores (ulcers) in mouth, nose or vagina	____	redness on palms of hand, soles of feet or around nails	____
skin rash	____	hair loss	____
dry eyes and mouth (Sjogren's)	____	blue, patchy skin coloring (livedo)	____
color change of fingers and toes in the cold (Raynaud's)	____	finger tip ulcerations	____

Part C

high blood pressure	____	angina (chest pain on exertion)	____
infection (flu, cold, sinus infection, sort throat, pneumonia, or other)	____	cough or lung congestion	____
shortness of breath	____	pleurisy (chest pain on breathing)	____

Part D

nausea, vomiting, diarrhea	____	indigestion, gastritis, ulcer	____
abdominal pain	____	menstrual period changes (more pain, heavy flow or no flow)	____

Part E

joint pain	____	joint stiffness	____
joint inflammation (redness, warmth, swelling)	____	pains or weakness in muscles	____

Part F

fever (temperature_______°)	____	swollen glands	____
urinary symptoms (burning or pain while urinating; blood in urine)	____		

Appendix F2

Weekly Lupus Symptoms Clusters Derived from Factor Analyses

Revised Scale & Items		Cronbach's Alpha Night 1	Night 7	Night 14
Pain Symptoms:				
joint pain joint inflammation joint stiffness	muscle pain or weakness headache	0.89	0.93	0.91
Skin Symptoms:		0.80	0.82	0.77
skin rash finger tip ulcerations redness on palms of hands, soles of feet, around nails	livedo (blue, patchy skin) Raynaud's (fingers, toes change color in the cold Sjogren's (dry eyes, mouth)			
Chest Symptoms:		0.89	0.88	0.90
shortness of breath cough or lung congestion pleurisy	angina ulcers in mouth, nose, or vagina			
Gastrointestinal Symptoms:		0.82	0.73	0.81
nausea, vomiting, diarrhea abdominal pain indigestion, gastritis, ulcer	infection (cold, flu, sinus, pneumonia, other) headache			
Neurological Symptoms:		0.79	0.66	0.57
memory loss, problems with thinking numbness, tingling, weakness or paralysis in arms or legs vision problems or abnormalities				
Psychological Symptoms:		0.80	0.73	0.77
mood swings anxiety depression				
Omitted items:				
seizure high blood pressure menstrual period changes burning or pain while urinating, blood in urine	fever hair loss swollen glands			

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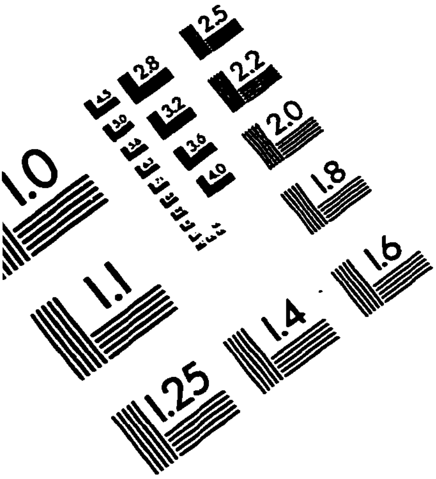
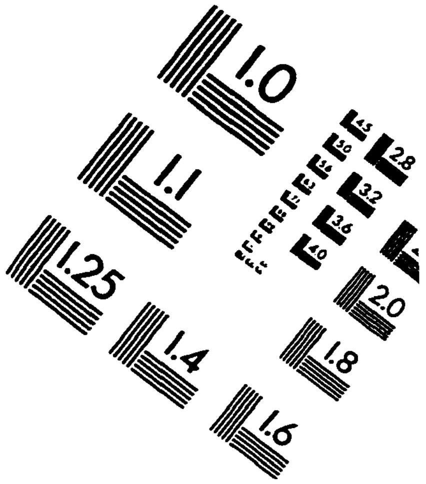
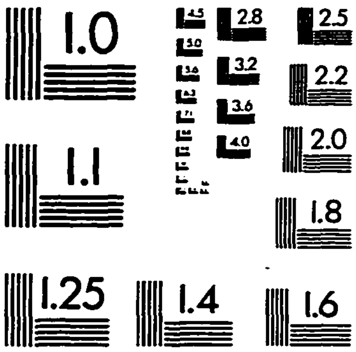
IMAGE EVALUATION TEST TARGET (QA-3)







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