

PSYCHOLOGICAL PROFILES IN AUTOIMMUNE DISEASE:
RELATIONSHIP TO DEMOGRAPHIC, DIAGNOSTIC, DISEASE ACTIVITY
AND SOCIAL SUPPORT MEASURES

By

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TABLE OF CONTENTS

	<u>Page</u>
LIST OF TABLES	iii
LIST OF FIGURES	iv
ABSTRACT	v
CHAPTER	
1 INTRODUCTION	1
Systemic Lupus Erythematosus	1
Sjögren’s Syndrome, Scleroderma, and Polymyositis	3
Antinuclear Antibody Positive Patients	4
Psychological Distress and Illness	5
Disease-Related Fatigue	7
Disease-Related Pain	9
Cluster Profiling	10
Illness Burden and the Immune Response	11
Social Support	13
Study Rationale	14
Aims	16
Hypotheses	17
2 METHODS	19
Participants	19
Procedure	20
Measures	21
Analyses	22
3 RESULTS	24
4 DISCUSSION	29
REFERENCES	36
BIOGRAPHICAL SKETCH	43

LIST OF TABLES

<u>Table</u>		<u>page</u>
2-1	Diagnostic breakdown of demographic information	19
3-1	Description of response profiles	25
3-2	Crosstabulation matrix of response profiles across diagnostic categories	26
3-3	Values for biological markers of disease activities	27

LIST OF FIGURES

<u>Figure</u>	<u>page</u>
1-1 Preliminary four-cluster solution representing psychological profiles in autoimmune disease patients	16
3-1 Replication four-cluster solution representing psychological profiles in autoimmune disease patients	24

Abstract of Dissertation Presented to the Graduate School
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Autoimmune diseases (AD) are characterized by chronic inflammation that can affect a variety of tissues in systemic or organ-specific forms. The challenges inherent to managing a chronic medical illness place individuals at greater risk for psychological distress, which could lead to deleterious effects on immune and neuroendocrine functioning and contribute to disease progression. Relatively little is known about variations in psychological function and the degree to which heterogeneity exists across a variety of autoimmune diseases. Further, the differential contributions of disease-related factors and psychological function to illness response remain unclear. Using a cluster analytic approach, this study determined homogenous psychological subgroups in a sample of 393 rheumatology outpatients referred to an autoimmune disease clinic for suspected AD. Participants included individuals diagnosed with an AD as well as individuals testing positive for anti-nuclear antibodies (ANA positive). Psychological subgroups were determined empirically based on visual analogue measures of depression, anxiety, anger, confusion, pain, and fatigue. Psychological response profiles

were subsequently examined in relation to demographic variables, diagnostic category, physician rated and immune measures of disease activity, and perceived social support. Results of the study provide support for substantial heterogeneity across in psychological function and illness response across the AD sample and within specific diagnostic groups. Psychological response profiles did not vary with respect to demographic variables, diagnosis, serological markers of disease activity, or physician-rated disease activity. Higher levels of perceived social support were associated with lower levels of mood disturbance and symptom reporting. Results suggest that personality, psychological, and/or social support factors may be stronger determinants of response to illness.

CHAPTER 1 INTRODUCTION

Autoimmunity refers to a breakdown in the immune system's ability to maintain self-tolerance, resulting in an immune response directed against self-components of the body. Autoimmune diseases (AD) are characterized by chronic inflammation in which the rate of tissue damage exceeds the body's ability to repair the damage. There is wide variability across ADs in the tissues that are attacked and specific symptoms caused. Although an understanding of the mechanisms responsible for maintaining tolerance exists, the specific factors contributing to the pathogenesis of AD remain largely unknown (Parham, 2000). It is generally accepted that the cause of any given AD is multifactorial and that environmental and genetic factors play a role in susceptibility (Tizard, 1995).

Autoimmune diseases are relatively common, affecting 2% to 3% of the population of developed countries (Parham, 2000) and 5% to 7% of adults in Europe and North America (Tizard, 1995). Two thirds of those affected are women. ADs can generally be divided into two types: organ-specific, where the immune response is directed toward a target antigen that is specific to a single organ or gland, and systemic, which involves a response directed across a broad array of organs and tissues (Kuby, 1991).

Systemic Lupus Erythematosus

Systemic lupus erythematosus (SLE) is a prototypical AD in which almost every tissue or organ may be affected. Its diagnosis depends on multisystem involvement and

the presence of autoantibodies, which together form the diagnostic criteria for SLE (Tan et al., 1982). Systemic lupus erythematosus is thus a syndrome, rather than single disease entity, that exhibits considerable variation in disease manifestations between individual patients. The course of SLE generally involves periods of intense flares and periods of remission (Parham, 2000).

The overall prevalence of SLE varies between studies from 12.0 to 50.8 with an average of about 40 per 100,000 individuals (Hopkinson, Doherty, & Powell, 1994). The highest prevalence is found in African American females at a rate of 200 per 100,000. The incidence of lupus has been reported between 2.0 and 7.6 new cases per 100,000 per year (Johnson, Gordon, Palmer, & Bacon, 1995). It is evident that sex has a major influence on the likelihood of developing SLE, with a 90% female predominance over males (Rus & Hochberg, 2002). The predominance of female SLE patients is not well understood, although hormonal factors are believed to play an important etiological role (Tizard, 1995).

Systemic lupus erythematosus is generally diagnosed according to the American College of Rheumatology's revised (Hochberg, 1997) criteria for SLE. The criteria include 11 items, 5 of which are composites of one or more abnormalities. In order to meet criteria for a diagnosis of SLE, patients must fulfill at least 4 criteria; however, no single criterion is essential (Wallace & Hahn, 2002). Laboratory diagnosis of SLE focuses to a large extent on antinuclear antibodies (Kuby, 1991). The absence of a clearly defined diagnostic marker for SLE contributes to the diagnostic challenge and can place patients at risk for misdiagnosis.

The wide variation in disease manifestations across individuals with SLE contributes to the challenge of developing a uniform system for assessing level of disease

activity. Consequently, the assessment of disease activity in SLE patients remains inconsistent within the rheumatology field. Over 60 systems for assessing disease activity exist, and agreement on a definition for SLE activity has not been achieved. In the United States, the most commonly used assessment system for disease activity is the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI; Bombardier, Gladman, Urowitz, Caron, & Chang, 1992), whereas in Europe, the British Isles Lupus Assessment Group (BILAG; Symmons et al., 1988) system predominates (Wallace & Hahn, 2002).

The economic impact of SLE has been estimated at a mean annual direct and indirect per patient cost of \$10,530 in the United States in 1991 (Gironimi et al., 1996). Given the marked rise in health care costs in the last decade and an average prevalence of about 40 per 100,000, this translates into considerable annual health expenditure. In addition to growing health care costs, the economic impact of SLE is expected to rise exponentially as the percentage of African Americans (presently at 12.9%) and Hispanics (presently at 12.5%) continues to grow faster than the Caucasian population (U.S. Census Bureau, 2000).

Sjögren's Syndrome, Scleroderma, and Polymyositis

A number of patients referred to specialists for suspected SLE are ultimately diagnosed with a different AD or are determined to have antinuclear antibodies (ANA) but not meet criteria for a specific AD. Among the systemic autoimmune conditions that share symptom overlap with SLE are Sjögren's syndrome, scleroderma, and polymyositis. Similar to SLE, these conditions involve a response mounted by the immune system against tissues in the body. In the case of Sjögren's syndrome, the immune system targets the salivary and lacrimal glands, leading to dryness in the mouth and eyes and complications including severe dental decay and corneal damage. The

female to male ratio is 9:1, and the overall prevalence for Sjögren's is 3% (Berkov, Beers, & Burs, 1999). Scleroderma, also known as systemic sclerosis, is an autoimmune condition involving overproduction of collagen that results in abnormal growth of connective tissues that support the skin and internal organs. Scleroderma occurs at a rate 7-12 times greater in females than males (National Institute of Arthritis and Musculoskeletal and Skin Diseases [NIAMS], 2001). Polymyositis is a connective tissue disorder characterized by inflammation and degenerative changes in muscles. Over time, this damage leads to symmetric weakness and muscle atrophy. This may be commonly associated with severe interstitial lung disease, which can rapidly lead to death. The female to male ratio is 2:1 with 2 to 10 new cases per one million (Berkov et al., 1999).

Antinuclear Antibody Positive Patients

Antinuclear antibody testing is one of several tests commonly ordered when a patient in primary care settings complains of chronic low energy, arthralgias, and myalgias (Blumenthal, 2002). Most patients referred to clinics specializing in rheumatologic or autoimmune conditions for suspected SLE have antinuclear antibodies. Antinuclear antibody testing is often used to screen for a diagnosis of lupus but has very low specificity (Illei & Klippel, 1999). Conversely, the absence of a positive ANA largely excludes the diagnosis of SLE as less than 4% of lupus patients have a negative ANA. In addition, up to 20% of healthy, asymptomatic individuals test ANA positive (Wallace & Hahn, 2002). Thus, many patients who test positive for ANA do not receive a diagnosis of SLE.

Although some ANA positive patients are diagnosed with an alternate autoimmune disorder or another condition, others receive no diagnosis. Blumenthal (2002) reported that many patients testing positive for ANA ultimately receive a

diagnosis of fibromyalgia syndrome (FMS) or an alternative pain syndrome. He argued that the prevalence of FMS is at least 20 times higher than that of lupus, which reduces the likelihood that a positive ANA will result in a diagnosis of lupus. Smart, Waylonis, and Hackshaw (1997) found that in a sample of 66 FMS patients, 20 (30%) were ANA positive.

Al-Allaf, Ottewell, and Pullar (2002) investigated whether ANA positive FMS patients developed other symptoms of connective disease over a 2- to 4-year follow-up period compared with age- and sex-matched ANA negative FMS and osteoarthritis (OA) patients. The ANA positive rates (12/137 [8.8%] in FMS and 20/225 [8.9%] in OA patients) were similar in both groups. At final assessment, one patient from the ANA positive FMS group was diagnosed with SLE, one patient from the ANA negative FMS group was diagnosed with Sjögren's syndrome, and one OA patient developed rheumatoid arthritis (RA). These results indicated that ANA status is not a good predictor of future development of AD. The ANA positive population, in the absence of AD, represents a unique and poorly defined group of patients. These patients range from asymptomatic to those suffering from FMS or an alternate pain condition.

Psychological Distress and Illness

The psychological aspects of SLE have not received extensive attention and remain poorly understood despite estimated rates for neuropsychiatric problems ranging from 33% to 60% and affective problems from 50% to 80% (Dobkin et al., 1998). Psychological distress, which includes depressed or anxious mood, occurs commonly in medical disorders and has a significant effect on quality of life and coping with disease (Adams, Dammers, Saia, Brantley, & Gaydos, 1994). Psychological distress represents patients' interpretations of stress and their perceived impact (Ward, Marx, & Barry, 2002)

and can be considered an intermediate measure in the relationship between stress and illness. Distress can impact health both indirectly, through health behaviors (e.g., compliance to medical regimens, poorer sleep, poorer nutrition) or directly through alterations in the central nervous, immune, endocrine, and cardiovascular systems (Kiecolt-Glaser, McGuire, Robles, & Glaser, 2002a).

Physical health problems, particularly those that are chronic, are considered a significant risk factor for depression (Zeiss, Lewinsohn, Rhode, & Seeley, 1996). Many of the ADs, such as SLE, present a course of unpredictable symptom flares and remissions. A diagnosis of AD requires adjusting to a new array of medical, social, psychological, vocational, and financial challenges and stressors. Depression is the most common psychiatric problem in patients with SLE. In a review of the literature, Giang (1991) found that 31% to 52% of lupus patients who underwent a structured or semi-structured interview were experiencing depression. The factors contributing to the etiology and maintenance of depression in lupus patients are unclear and likely involve numerous biopsychosocial factors (Iverson, Sawyer, McCracken, & Kozora, 2001).

Elevated levels of psychological distress have also been reported in scleroderma and Sjögren's syndrome patients. Valtysdottir, Gudbjornsson, Lindqvist, Hallgren, and Hetta (2000) examined levels of anxiety, depression, well-being, and symptoms in 62 Sjögren's patients compared with a group of healthy controls and a group of patient controls with RA. The results indicated significantly higher levels of anxiety and depression, and reduced physical and mental well-being in Sjögren's patients compared with healthy controls. The Sjögren's patients also reported significantly more symptoms than RA patients.

Matsura and colleagues (2003) evaluated 50 patients with scleroderma for factors associated with depressive symptoms using the Beck Depression Inventory (BDI; Beck, 1967). Forty-six percent of the sample reported depressive symptoms ranging from mild to severe. Regression analyses revealed that high levels of hopelessness and low sense of coherence (coping ability and resilience in the face of stress) were the best predictors of depressive symptoms in this sample.

Psychological distress affects morbidity in patients with comorbid medical illness in several ways. As Iverson et al. (2001) highlighted, depression can greatly impact functional status and degree of disability in the areas of social, occupational, educational, and recreational functioning. Depression has also been shown to influence patients' adherence to medical regimens. In addition to influencing overt behavioral functioning, there is also evidence that psychological distress is directly related to disease activity (Dobkin et al., 1998). However, it remains unknown as to whether psychological distress leads to increased SLE activity or if disease activity leads patients to become more depressed or anxious.

Disease-Related Fatigue

Fatigue is a commonly reported symptom in medical patients and one of the most widely reported symptoms in SLE. Zonana-Nacach and colleagues (2000) found that 85.7% of 223 participants with SLE reported fatigue; and Krupp, LaRocca, Muir, and Steinberg (1991) found fatigue to be reported in 80% of their SLE sample. Disabling fatigue is also a prominent feature of primary Sjögren's syndrome (Lwin, Bishay, Platts, Booth, & Bowman, 2003). Fatigue is a primary contributor to functional disability and visits with health care providers. Belza, Henke, Yelin, Epstein and Gilliss (1993) reported

a significant positive association between fatigue levels in RA patients and frequency of visits to their rheumatologists.

Numerous factors have been associated with fatigue in SLE, including level of aerobic fitness, pain, medications, sleep problems, and clinical and laboratory features of SLE (Zonana-Nacach et al., 2000). Depression also is related strongly to fatigue (De Rijk, Schreurs, & Bensing, 1999) and a positive association between fatigue and depression has been reported in patients with SLE (Krupp et al., 1991). Although fatigue is sometimes viewed as a reflection of disease activity, it often persists despite decreases in disease activity, indicating that additional factors likely play a role in maintaining fatigue levels.

Studies investigating fatigue and disease activity have provided inconsistent findings for a biologic explanation for fatigue. Bruce, Mak, Hallett, Gladmann, and Urowitz (1999) found disease activity and damage accounted for only 4.8% and 4%, respectively, of the variance in fatigue scores in a sample of 81 lupus patients. Several studies (e.g., Tench, McCurdie, White, & D'Cruz, 2000; Zonana-Nacach et al., 2000) have shown weak associations between fatigue and disease activity. In contrast, Tayer, Nicassio, Weisman, Schuman, and Daly (2001) found that in a cross-sectional analysis of 81 SLE patients, disease status, helplessness, and depression are independently significant predictors of fatigue. In a longitudinal design testing the same variables, only disease status predicted future fatigue levels. Overall, these findings support the possibility that a combination of disease and psychosocial factors are capable of influencing fatigue levels.

Several investigations have provided support for the role of psychological distress in the experience of fatigue in SLE. McKinley, Ouellette, and Winkel (1995)

demonstrated that while disease activity did not exert a direct effect on fatigue, it did influence depression and sleep disruption, which may, in turn, exert a more direct effect on fatigue. Omdal, Waterloo, Koldingsnes, Husby, and Mellgren (2003) found in a sample of 57 SLE patients that affective and personality states as well as mental health status were significant predictors of fatigue. Fatigue, as with pain, appears to be a multidimensional construct with a significant psychological component.

Disease-Related Pain

Pain is among the most common reasons individuals seek medical care. It accounts for substantial levels of functional disability and contributes greatly to overall illness burden (Turk & Melzack, 1992), including visits to health care providers, medication expense, and work-related disability. Pain has been consistently linked with negative mood states (Robinson & Riley, 1999) and can enhance stress-related hormones and immune dysregulation (Kiecolt-Glaser, McGuire, Robles, & Glaser, 2002b). It appears that this triad of symptomology involving fatigue, pain, and distress (e.g., depression, anxiety) creates a negative spiral resulting in increasing levels of disability.

Pain related to arthritis and arthralgias occurs in 95% of lupus patients at some point in the course of their illness (Schur, 1996). The relationship between pain and fatigue in chronic pain conditions has been firmly established (Belza et al., 1993; Wolfe, Hawley, & Wilson, 1996). Coping with unpredictable and severe amounts of pain requires additional physical and emotional endurance, which may further deplete energy and coping resources in lupus patients. Further, reduced levels of activity could result in muscle deconditioning, which, in turn, could contribute to increased levels of perceived fatigue (Belza et al., 1993; Robb-Nicholson et al., 1989) and increased level of pain.

Pain is a defining symptom in polymyositis and may also be important in scleroderma. Benrud-Larson and colleagues (2002) investigated the frequency and impact of pain, symptoms of depression, and social network characteristics on physical functioning and social adjustment in 142 patients with scleroderma. Sixty-three percent of patients reported mild or greater pain, and half of the sample reported mild or greater levels of depression. The results showed that pain was the strongest predictor of physical function, and depressive symptoms accounted for the greatest amount of variance in social adjustment. Their findings suggest that pain and depressive symptoms are important determinants of quality of life in scleroderma patients.

Cluster Profiling

Empirical approaches to classifying homogenous psychological subgroups have been used extensively in chronic pain patients. This approach originated as an effort to counter assumption that pain patients represent a homogenous group and to determine whether treatment response could be improved by tailoring treatments to subgroups of patients based on specific characteristics (Turk & Okifuji, 2002). Using the Multidimensional Pain Inventory (MPI; Kerns, Turk, & Rudy, 1985), Turk and Rudy (1988) cluster analyzed patients' responses and found three homogenous groups of pain patients: (a) dysfunctional, (b) interpersonally distressed, and (b) active copers. This classification system has been replicated in chronic low back pain (CLBP), head pain, FMS, and temporomandibular disorder (TMD). Additionally, subgroup differences were found in response to treatment, suggesting that the use of classification systems to tailor treatment approaches to specific subgroups may improve treatment efficacy.

The Minnesota Multiphasic Personality Inventory (MMPI) has been found to be highly consistent in identifying subgroups within a variety of chronic pain populations,

such as headache (Robinson, Geisser, Dieter, & Swerdlow, 1991), chronic musculoskeletal pain (Riley, Geisser, & Robinson, 1999) and TMD (Velly, Philippe, & Gornitsky, 2002). These findings provide additional evidence to suggest that within broad categories of pain conditions, distinct subgroups exist. Identification of such subgroups in AD could enhance our understanding of variability in responses to illness and its subsequent treatment.

Illness Burden and the Immune Response

In AD, the relationships between emotions, psychological distress, immune and neuroendocrine functioning, and disease manifestations are of particular interest. There is considerable evidence to suggest that emotional states can produce alterations in the immune response. It is currently accepted that the brain and the immune system share bidirectional communication and exert important regulatory control over one another. The existence of such neural-immune interactions provides a pathway by which psychological processes can influence and be influenced by immune function (Maier, Watkins, & Fleshner, 1994). Additionally, immunological alterations have been reported across a wide range of psychiatric disorders (Kiecolt-Glaser et al., 2002a).

A growing body of evidence suggests a role for psychological distress in inducing, exacerbating, and affecting outcomes in SLE (Shapiro, 1997). Depressed immune responsiveness is characteristic of patients with SLE. Research has shown that psychological distress further dampens the immune response via activation of the hypothalamic-pituitary-adrenal (HPA) axis (Ader, Cohen, & Felton, 1995), which may result in more active disease. A 1999 study by Pawlak and colleagues demonstrated a distinct difference between the stress response of SLE patients and healthy controls following a stressful task (public speaking). Systemic lupus erythematosus patients

showed significantly less pronounced increases in NK cell numbers compared to the controls. Additionally, NK cell activity increased in the controls but not in the SLE patients, indicating a blunted immune response to acute stress.

Inflammation is linked to a variety of conditions associated with aging (Kiecolt-Glaser et al., 2002b) and is an important feature in AD. Chronic inflammation and immune challenge associated with illness serve as physiologic stressors leading to activation of the HPA axis. Dysregulation of inflammatory mediators is commonly observed in ADs and has also been shown to correlate with psychological variables, such as depression. The majority of research to date in this area has focused on pro-inflammatory cytokines. Cytokines are low molecular weight protein substances released by cells that serve as intercellular signals to regulate the immune response to injury and infection (Parham, 2000). Cytokines have been proposed as the messengers between the brain and the immune system (Maier et al., 1994).

Several studies have shown that patients with SLE display an altered cytokine profile (Jacobs et al., 2001). One pro-inflammatory cytokine that has received increased attention in a variety of medical and psychiatric populations is interleukin-6 (IL-6). Studies of the role of IL-6 in SLE have lead to relatively uniform results. Circulating IL-6 levels are elevated in patients with SLE, compared to those with inactive disease and healthy controls (Lacki, Leszczynski, Kelemen, Muller, & Mackiewicz, 1997). IL-6 also has shown a consistent relationship with depression across a number of studies. Maes and colleagues (1995) found elevated levels of IL-6 and soluble IL-6 receptors (sIL-6R) in patients with major depression (MD), whether active or in remission, suggesting that the upregulated production of IL-6 may be a trait marker for MD.

Some researchers have proposed that psychological stress can instigate the inflammatory response. According to Black (2003), the inflammatory response is contained within the psychological stress response, which evolved later. The same neuropeptides mediate the body's response to both stress and inflammation. Cytokines evoked by either a stress or inflammatory response may utilize similar pathways to signal the brain, signaling a cascade of hormones, neuropeptides, and cytokine activity.

Negative affect has been identified as a key pathway for modifying immune processes. There is preliminary evidence that anxiety and depression enhance the production of pro-inflammatory cytokines (Kiecolt-Glaser et al., 2002a). Immune modulation by psychosocial stressors and/or interventions can lead to health changes. Pro-inflammatory cytokines, such as Il-6, stimulate the release of acute phase reactants from the liver. Acute phase proteins, such as C-reactive protein (CRP) and complement proteins (C3 and C4) are part of the body's innate immune inflammatory response to infection.

Berk, Wade, Kuschke, and O'Neill-Kerr (1997) compared levels of acute phase proteins (C3, C4 and CRP) in depressed versus nondepressed subjects according to DSM-III-R criteria and found significant elevations in C4 and CRP in the depressed group. These findings suggest the possibility of an underlying relationship between depression and inflammation in autoimmune patients. Furthermore, many physicians now believe that CRP can be used as an aid in assessing the risk of cardiovascular and peripheral vascular disease. The relationships among psychological factors and acute phase proteins have not been previously reported in AD populations.

Social Support

The benefits of social support have been given extensive consideration throughout the chronic illness literature. Social support is negatively correlated with psychological

distress and has been shown to influence health behaviors, such as seeking medical care (Cohen, 1988). McCracken, Semenchuk, and Goetch (1995) found that good social support was related to perceptions of health and that seeking social support was associated with lower levels of pain, physical disability, psychological distress, and depression. Furthermore, social support can serve as a buffer during both acute and chronic stressors, thereby protecting the individual against immune dysregulation (Kiecolt-Glaser et al., 2002a).

Two studies (Bae, Hashimoto, Karlson, Liang, & Daltroy, 2001; Sutcliffe et al., 1999) reported that higher levels of social support were associated with better physical and mental well-being in SLE patients. However, there are no studies to date that have examined the role of social support as a buffer against immune dysregulation in SLE, scleroderma, Sjögren's syndrome, polymyositis, or ANA positive patients.

Study Rationale

The participants in this study shared common complaints and symptoms characteristic of suspected AD. Following medical evaluation, individuals were placed into a variety of categories ranging from ANA positive to having been diagnosed with one of many ADs. The assumption of heterogeneity in such a diverse population might lead to generic treatment approaches aimed at the "average" or "typical" patient. Another pitfall might be to assume that more severe illness equals more distressed or that adjustment to illness was similar across a variety of conditions. The purpose of this study was to explore the possibility that homogenous subgroups exist based on specific shared qualities. Identifying such subgroups offers the possibility to better understand variability in response to illness and to tailor treatment to subgroups based on specific characteristics.

Relatively little is known about how individuals with ADs such as SLE, scleroderma and polymyositis and ANA positive patients vary with respect to psychological function and adjustment to illness. The level of heterogeneity across individuals, disease categories, and illness severity remains to be determined. To date, there are few reports describing the psychological characteristics of ANA positive patients. Across conditions, one might expect that those posing a greater threat to mortality, quality of life, and function would lead to higher levels of distress and greater coping challenges. Within disease categories, factors such as premorbid psychological status and disease severity could play important roles in current psychological adjustment and status.

There are few studies to date that have attempted to elucidate the relationships among psychological factors and inflammatory mediators in ANA positive, SLE, and related autoimmune conditions. Further, no studies have investigated the relationship between psychosocial factors, pain, fatigue, and acute phase proteins in this population. Finally, although physician-rated measures of disease activity have been compared to individual psychological and self-rated symptoms, such as pain and fatigue, in SLE patients, the relationship between physician-rated disease activity and multivariate psychological response profiles has not been previously reported. The aim of this study was to contribute to the understanding of these relationships using an empirical clustering approach to examine how these variables are related.

Using a cluster-analytic approach, a pilot study was conducted to determine whether unique patterns of psychological (depression, anxiety, confusion, and anger) and symptom (pain and fatigue) reports exist within an AD sample. The preliminary study was conducted on 279 participants to determine whether patients presenting in an AD

clinic could be classified into subgroups based on unique psychological response profiles. The cluster analysis revealed a four-cluster solution. The four-cluster solution was chosen because it provided better group separation and more parsimonious interpretation. Figure 1-1 provides a graphical representation of the four clusters.

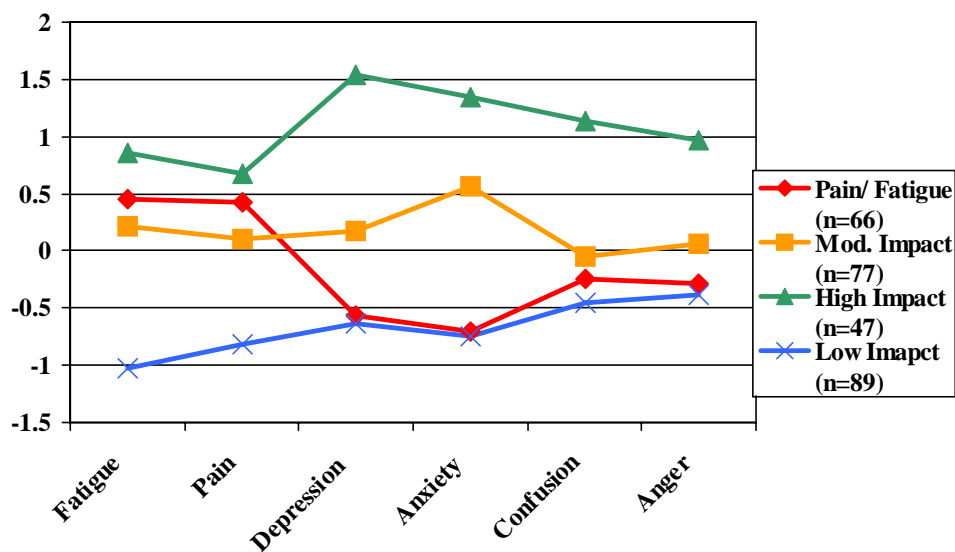


Figure 1-1. Preliminary four-cluster solution representing psychological profiles in autoimmune disease patients

The first cluster, “Pain/Fatigue” (n = 66), displayed moderate levels of pain and fatigue and low levels of distress. The “Moderate Impact” cluster, comprised of 77 participants, is characterized by moderate levels of pain, fatigue, and distress with an elevation in anxiety. The “High Impact” cluster (n = 47) displayed high distress and symptom levels, and the “Low Impact” cluster (n = 89) demonstrated low levels of symptoms and distress. Based on this pilot data indicating the presence of four distinct psychological response profiles in the AD sample, several aims were developed.

Aims

The initial aim of this study involved replicating the four-cluster solution using a larger sample. Secondly, this study sought to determine whether clusters are associated

with demographic variables, including race, age, sex, and illness duration. Next, the concordance among psychological response profiles and diagnostic categories (ANA positive, SLE, Sjögren's, polymyositis, and scleroderma) was examined. The relationship between psychological response profiles and biological markers was also examined to assess whether psychological response profiles predict serological markers of disease activity (urinary IL-6, CRP, C3, C4, albumin, and prealbumin). A secondary objective included determining whether psychological response profiles predict physician-rated levels of disease activity in SLE patients. The relationship between psychological response profiles and SLE Disease Activity Index (SLEDAI; Bombardier et al., 1992) was examined. Finally, the relationship between psychological response profiles and perceived social support was assessed.

The results of this study provided preliminary evidence indicating whether psychological response profiles were determined primarily by disease process, indicating a pathophysiological basis for psychological functioning, or by psychosocial factors and predisposing personality traits, suggesting a psychological basis for individual responses to physical illness. Although, in reality, the answer likely lies in the middle of these extremes, this study provided insight into the differential contributions of these opposing hypotheses.

Hypotheses

- The same four-cluster solution found in the pilot study was repeated in a larger autoimmune disease clinic sample.
- Equal representation of diagnosis across clusters was supportive of the notion that predisposing factors (personality, social support, etc.) predict psychological response to illness. A higher frequency of diagnosed AD in the more distressed profiles was supportive of disease severity determining psychological response.

- Response profiles reflecting higher levels of pain, fatigue, and distress will be associated with increased activation of serological markers of disease activity
 - Higher levels of urinary IL-6, CRP, albumin, and prealbumin
 - Lower levels of complement components (C3 and C4)
- Response profiles reflecting higher levels of pain, fatigue, and distress will be associated with higher levels of physician-rated disease activity in SLE patients, supporting the notion that disease contributes to psychological response. Absence of significant differences between response profiles on disease activity scores would support the view that psychological response to illness may be independent of specific pathological processes.
- Response profiles reflecting higher levels of pain, fatigue, and distress will be inversely associated with levels of perceived social support, thereby supporting the notion that greater social support serves as a buffer against the harmful effects of illness on psychological well-being.

CHAPTER 2
METHODS

Participants

Participants in this study were 393 rheumatology outpatients recruited from the Autoimmune Disease Clinic at Shands Hospital in Gainesville, Florida. The mean age of the patients was 44.3 (SD = 13.7), and the mean duration since diagnosis was 8.0 (SD = 7.6) years. Patients were predominantly female (90.1%), and the majority of patients were Caucasian (64.1%). Patients were categorized according to primary diagnosis, although it should be noted that many patients met criteria for more than one autoimmune disorder. The largest proportion of patients was diagnosed with SLE (43%), followed by patients who were ANA positive (25.7%) but did not meet criteria for an autoimmune disease diagnosis. Diagnostic information is presented in Table 2-1.

Table 2-1. Diagnostic breakdown of demographic information

Diagnosis	N	%	Duration	Edu	Age	Sex		Race		
			(yrs)	(yrs)	(yrs)	N (% total)		N (% total)		
			M (SD)	M (SD)	M (SD)	F	M	W	B	O
SLE	176	45	10.5 (8.4)	13.5 (2.4)	41.3 (12.8)	162.0 (41.2)	14.0 (3.6)	89.0 (22.6)	62.0 (15.8)	25.0 (6.4)
ANA POS	101	26	4.0 (4.5)	13.7 (2.5)	43.8 (13.7)	91.0 (23.2)	10.0 (2.5)	77.0 (19.6)	11.0 (2.8)	13.0 (3.3)
Sjögren's	26	7	6.8 (4.0)	14.0 (2.3)	52.8 (14.4)	24.0 (6.1)	2.0 (0.5)	25.0 (6.4)	1.0 (0.3)	0.0 (0.0)
SSC	22	6	8.2 (6.1)	12.8 (3.3)	53.8 (10.4)	19.0 (4.8)	3.0 (0.8)	16.0 (4.1)	6.0 (1.5)	0.0 (0.0)
Other	68	17	7.3 (8.3)	13.7 (2.4)	46.4 (13.8)	58.0 (14.8)	10.0 (2.5)	45.0 (11.5)	16.0 (4.1)	7.0 (1.8)
Total	393	100	8.0 (7.6)	13.6 (2.5)	44.3 (13.7)	354.0 (90.1)	39.0 (9.9)	252.0 (64.1)	96.0 (24.4)	45.0 (11.5)

Patients eligible for participation in this study were preselected based on participation in the large study examine factors contributing to the development of autoimmune disease (IRB#: 454). Patients were recruited by their treating physicians during routine medical visits. Eligibility was determined by each patient's treating physician according to necessary criteria. Eligibility criteria included being 18 years or older, English-speaking, literate, and possessing a minimum education level of 8th grade. Both males and females from all racial/ethnic backgrounds were included. Participation was also contingent upon ability to provide consent. Patients with cognitive, emotional, or physical problems believed to interfere with his or her ability to provide consent were not permitted to participate. Written consent for research participation was obtained at the conclusion of routine visits.

Procedure

Recruitment took place during routine medical visits. Eligible participants were approached by his or her rheumatologist or trained research staff regarding participation in the study. The informed consent form was verbally reviewed prior to obtaining patients' signatures to ensure complete understanding of their rights as research participants. Participation in this study did not interfere with routine rheumatologic care.

Following their routine rheumatology visit, staff members escorted participants to the General Clinical Research Center (GCRC) at Shands Hospital for clinical laboratory tests. In addition to clinical laboratory tests ordered by their rheumatologist, biological samples were obtained exclusively for research purposes. At this time, participants completed the psychosocial questionnaire packet, consisting of a battery of self-report paper and pencil questionnaires. Instructions for completing the questionnaire were

provided by a trained research assistant. The packet generally required 10 to 15 minutes to complete.

Measures

Standard demographic data were collected during each participant's initial assessment. Information related to medical diagnosis and disease duration was recorded for research purposes after patients provided informed consent to participate in the study.

Psychosocial Measures

The assessment of distress and symptom levels includes seven visual analogue scales (VASs). Respondents were asked to indicate their level of functioning in each of the assessed domains by drawing a vertical line through one point on a 100 mm linear analogue scale. Scores were obtained by manual measurement of the VAS responses and range from 0-100. Each domain is anchored by the following descriptors: "None" and "Worst Imaginable." The domains assessed by VASs in this study included depression, anxiety, anger, confusion, pain intensity, and fatigue.

The use of VASs for assessing psychological distress and symptom domains in a brief format is not uncommon. The pain VAS (Price, McGrath, Rafii, & Buckingham, 1983) is a 100-mm line anchored by the descriptors, "No pain" to "Worst Pain Imaginable." Adequate reliability and validity have been reported (Price et al., 1983).

Social support was measured using the Perceived Social Support Scale (PSSS; Blumenthal, Burg, Barefoot, Williams, Haney, & Zimet, 1987). The PSSS is a 12-item scale employing a 7-point Likert response scale ranging from 1 (Very Strongly Disagree) to 7 (Very Strongly Agree). This scale addresses perceived support from family, friends, and significant others. Test-retest reliability was reported as 0.85 and Cronbach's coefficient alpha was 0.88 (Blumenthal et al., 1987).

Physician-Rated Disease Activity

The SLE Disease Activity Index (SLEDAI; Bombardier et al., 1992) is a physician-rating scale consisting of 24 descriptors associated with nine organ systems. Clinical and laboratory measures of SLE activity are included. Items are weighted according to severity and life-threatening items receive greater weights. The weighted items are summed to obtain an overall score. The range for possible scores is from 0 to 105. The SLEDAI has been validated and shown to be sensitive to changes over time (Fortin et al., 2000; Petri, Hellman & Hochberg, 1992).

Biological Measures

Urinary levels of IL-6 was measured using Enzyme-Linked Immunosorbent Assay (ELISA), an established method for determining cytokine levels. High-sensitivity CRP, C3, C4, albumin, and prealbumin will be measured by nephelometry on a BN Prospec II (Dade Behring) nephelometer. Nephelometry is a technique that uses analysis of light scattered by liquid to measure the size and concentration of particles in the liquid.

Analyses

All data analyses were performed using SPSS for windows (Version 11). Hierarchical cluster analysis (Ward's Linkage) was employed to identify distinct subgroups underlying the data structure. In order to validate the stability of the cluster solution, the overall sample was split into halves using a random selection function within the statistical software. The four-cluster solution was replicated in both halves, lending further support to the validity of these four response profiles across AD patients.

Following the empirical derivation of response profiles, the assigned cluster membership value (1-4) was used in subsequent analyses. Nonparametric chi square analyses and analyses of variance were the principle statistics used in these analyses. For

all ANOVAs, significant F-tests were followed by post-hoc analyses using Tukey's HSD to evaluate pairwise comparisons between response profiles on the dependent variable.

Statistical significance was set at an alpha value of .05 for all analyses.

CHAPTER 3 RESULTS

This study was based on the empirical determination of patient subgroups from the AD clinic based on the following scores: fatigue, pain intensity, depression, anxiety, anger, and confusion. Complete data for this analysis was available for 374 participants. Results of the hierarchical cluster analysis revealed a four-cluster solution (Figure 3-1), which was determined quantitatively based on the percentage change in the agglomeration coefficients.

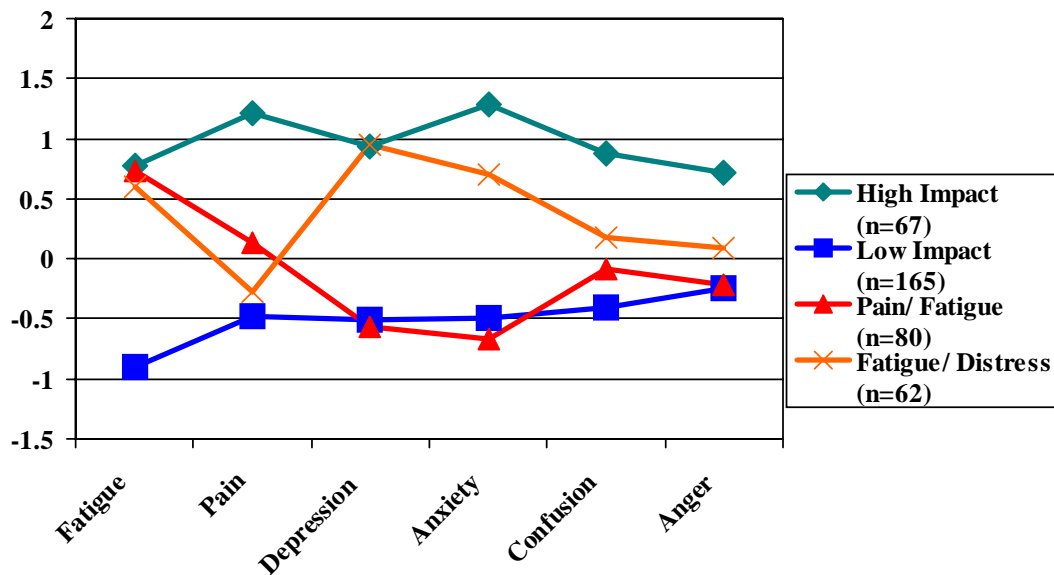


Figure 3-1. Replication four-cluster solution representing psychological profiles in autoimmune disease patients

Subgroups represent relatively unique response profiles derived from the multivariate combination of symptom and mood measures. Table 3-1 provides a summary of the response profiles. The “High Impact” cluster (N = 67) is characterized by

high scores across all measures with particularly high (>1 SD from mean) elevations in pain and anxiety. The “Low Impact” cluster (N = 165), the highest frequency cluster, reflects low levels for all mood and symptom variables. The “Pain/Fatigue” cluster (N = 80) profile reflects significant fatigue, moderate pain and relatively low levels of distress and confusion. The “Fatigue/Distress” cluster (N = 62) is characterized by high levels of fatigue, depression, and anxiety. The increase in sample size from the pilot study (N = 279) to the full sample (N = 374) resulted in an altered distribution of participants across the four clusters, whereby a larger proportion (44%) of participants fell in the profile cluster representing low symptom and distress levels.

Table 3-1. Description of response profiles

Cluster	N	Description
1	67	High impact
2	165	Low impact
3	80	Pain/Fatigue
4	62	Fatigue/Distress

Following the derivation of response profiles, a series of analyses were undertaken to examine whether profiles differed across demographic, diagnostic, and physiological variables. First, the relationship between response profiles and demographic variables was examined to determine whether race, sex, age, or illness duration predict psychological response profile. Nonparametric chi square analyses were used to examine the relationships of race and sex to response profiles. Results showed that racial background was proportionately distributed across the four psychological response profile membership, $\chi^2=5.76 (6), p = .450$. Chi-square results for sex were significant, $\chi^2=8.49 (3), p=.037$, indicating that men and women were disproportionately represented across clusters. Closer examination of the crosstabulation matrix revealed

that no males were present in the “Fatigue/Distress” cluster. However, given the small number of males (9.9%, N = 39) in the sample, this finding has limited interpretive value.

One-way analyses of variance (ANOVAs) were used to compare response profiles on age and duration since diagnosis. Response profile groups did not differ on age ($F(3,370) = 1.61, p = .188$) or duration since diagnosis ($F(3,320) = 0.81, p = .490$). Thus, current age and time elapsed since being diagnosed are not predictive of symptom and mood response profiles.

The second hypothesis concerned the concordance among psychological response profiles and diagnostic categories (ANA positive, SLE, scleroderma, Sjögren’s, and polymyositis, and other). The frequency of response profiles across diagnostic groups was assessed using nonparametric chi square tests. This analysis aimed to determine whether disease factors associated with a diagnosis of AD are associated with response profiles reflecting greater pain, fatigue and distress. The results revealed the proportionate distribution of diagnoses across the four response profiles, $\chi^2 = 5.24(12), p = .950$. This finding suggests that response profiles do not differ significantly between various autoimmune conditions (Table 3-2).

Table 3-2. Crosstabulation matrix of response profiles across diagnostic categories

Diagnosis	Response profile (N)				Total
	1	2	3	4	N (%)
SLE	28	71	36	29	164 (43.8)
ANA POS	18	48	19	14	99 (26.5)
Sjögren’s	3	12	5	5	25 (6.7)
SSC	3	10	6	2	21 (5.6)
Other	15	24	14	12	65 (17.4)
Total	67	165	80	62	374 (100.0)

The next series of analyses examined whether psychological response profiles represent varying levels of disease activity. ANOVAs were used to test for differences in

levels of disease activity as measured by a number of biological markers. Separate ANOVAs were conducted for urinary Il-6, hsCRP, C3, C4, albumin and prealbumin. A descriptive overview and results for these parameters is presented in Table 3-3.

Table 3-3. Values for biological markers of disease activities

Variable	N	Range	Mean	SD	F	Sig.
Il-6*	78	0.01 - 3683.50	433.56	792.15	0.932	0.430
HsCRP*	296	0.15 - 108.00	8.03	13.21	0.130	0.944
C3	297	24.10 - 261.00	116.65	34.40	2.180	0.091
C4	292	3.04 - 118.00	21.21	12.36	2.700	.046 ⁺
Prealbumin	221	10.40 - 60.40	25.95	8.61	0.695	0.556
Albumin	250	0.00 - 2048.00	51.64	211.69	0.336	0.799

IV = response profile group

* Values presented are based on raw data. Nonnormal distributions were transformed logarithmically for statistical analyses.

⁺ $p < .05$

Response profiles did not differ on mean levels of Il-6 ($F(3, 70) = 0.932, p = .430$), hsCRP ($F(3, 293) = .13, p = .944$) or C3 ($F(3, 294) = 2.18, p = .091$). Significant differences between groups were found for C4 ($F(3, 289) = 2.7, p = .046$). Post-hoc tests using Tukey's HSD revealed the "Low Impact" and "Pain/Fatigue" clusters differed significantly ($p = .045$) on C4 values. This finding has limited value because correcting for multiple comparisons suggests this significant finding could be due to chance. There were no differences between prealbumin ($F(3, 218) = .695, p = .556$) and albumin ($F(3, 247) = .336, p = .799$) levels between response profiles.

The collection of physician-rated SLE disease activity (SLEDAI) measures is limited to those patients carrying a diagnosis of SLE. Thus, patients diagnosed with SLE were selected to examine whether differences in total SLEDAI scores exist between response profile groups. The range for SLEDAI scores was 0 to 24 and the mean was 3.27 (SD=4.12). Forty-one percent of SLE patients received a SLEDAI score of greater

than or equal to four. Due to the significant positive skew of the distribution, a square root transformation was performed to normalize the data distribution. ANOVA revealed that SLEDAI scores did not differ significantly across response profiles ($F(3, 142) = .786, p = .504$).

The final hypothesis concerned the relationship between psychological response profiles and levels of perceived social support. Results of the ANOVA showed that psychological response profiles were associated with varying levels of social support ($F(3, 368) = 5.13, p = .002$). Post-hoc analyses revealed that the “Low Impact” cluster reported significantly ($p = .001$) higher levels of perceived social support than the “Fatigue/Distress” cluster.

CHAPTER 4 DISCUSSION

Unique subgroups of patients were determined empirically within a cohort of AD and ANA positive patients based on a similar response pattern. Psychological and symptom reporting profiles in this sample did not vary with respect to demographic characteristics, diagnostic categories, serological markers of disease activity, and physician-rated disease activity. Higher levels of perceived social support were associated with response profiles characterized by lower levels of mood and symptom reporting. The results of this study provide support for the presence of substantial heterogeneity in illness response and psychological functioning across a large sample of AD and ANA positive patients as well as within specific disease groups. Further, subgroups are independent of disease factors, including diagnosis, suggesting that personality, psychological, and/or social support factors are a stronger determinant of response to illness.

Variations in psychological functioning within this illness population were expected to span the continuum from well-adjusted to highly distressed participants. The results of this study bring attention to the sizeable number of patients who are experiencing elevated levels of subjective distress. Eighteen percent of participants fell within the “High Impact” cluster profile, and 38% were characterized by some elevations in symptoms and/or distress. These results signify the role of perceived symptom and distress in overall illness coping and quality of life. At the same time, it is important to

keep in mind that not all patients experiencing illness or symptoms reminiscent of a diagnosable disorder report compromised psychological functioning.

Cluster profiles were compared on a number of variables, including demographic, diagnostic, disease activity, and social support measures. Race, age, and illness duration were evenly distributed across cluster profiles, indicating that these variables are not associated with differences in psychological response profiles. These results are consistent with other studies that have demonstrated a lack of association between measures of distress and demographic characteristics. For example, in a sample of RA patients, VanDyke and colleagues (2004) found no significant relationship between anxiety and illness duration. Similarly, Alarcon and colleagues (2004) demonstrated in a cohort of 364 SLE patients that age and ethnicity were not associated with the physical and mental subscales of the SF-36. Results of this study did indicate a significant effect for sex when compared across clusters; however, the disproportionately small number of males in the sample limits the ability to interpret this finding.

Opposing hypotheses were presented with regard to the relationship between psychological profiles and diagnostic category. Across conditions, one might expect that conditions posing a greater threat to mortality, quality of life, and function would lead to higher levels of distress and greater coping challenges, thereby supporting that psychological response is determined to a large extent by disease severity. However, results demonstrated that response profiles were equally distributed across diagnostic categories, suggesting that coping profiles are independent of diagnosis. Equal representation of diagnoses across response clusters points to predisposing factors such as personality, social support, and coping style determining response profile membership.

This finding provides meaningful implications for the treatment of patients with the various diagnoses under consideration in this study. For example, physicians who are biased toward assuming that worse disease is related to poor psychological adjustment or that a positive ANA titer in the absence of a diagnosable AD should be less psychologically threatening to the individual are at risk for under- or over-interpreting psychological well-being based on disease threat or severity. The results of this study suggest that illness adjustment is not related to diagnosis. In fact, psychological functioning and/or perceived social support might be a more accurate predictor of how patients will respond to their illness.

In this study, it is not possible to determine the extent to which psychological response to illness is based on premorbid factors versus factors that are activated or influenced in the presence of illness. Support for the idea that premorbid psychological function plays an important role in response to illness has been demonstrated through investigations of neuroticism and self-reported adjustment. Costa and McCrae (1987) found that patients scoring particularly high on neuroticism tend to report higher levels of self-reported psychological and physical symptoms, without suffering from worse clinical outcomes. Given that psychological distress influences perceived quality of life, behaviors that can affect health outcome (e.g., exercise, diet, and use of alcohol, drugs, and nicotine), and response to illness, subjective distress levels are important to consider when illness is present, regardless of diagnosis.

Variations in psychological functioning were hypothesized to reflect differences in disease status as measured by serological markers of disease activity. This hypothesis was not supported. Response profiles characterized by higher levels of pain, fatigue, and distress were not associated with increased activation of serological markers of disease

activity. Symptom profiles are not accounted for by underlying disease processes and appear to be better explained by premorbid psychological factors. Statistical significance was achieved for complement protein C4 between the “Low Impact” and “Pain/Fatigue” groups; however, the relationship was not in the anticipated direction. This finding is most likely the product of statistical chance due to the number of serological tests conducted. In sum, the weight of the evidence does not support an association between serological markers of disease activity and response profiles.

Response profiles reflecting higher levels of pain, fatigue, and distress were not associated with higher levels of physician-rated disease activity in SLE patients, suggesting psychological response to illness may be independent of specific pathological processes. Another possible interpretation is that physician-ratings of disease activity are not congruent with patients’ perceptions of disease activity. Ward and colleagues (2002) found that changes in depression and anxiety were positively correlated with simultaneous changes in the patient global assessment of SLE activity but not with changes in SLEDAI scores. Furthermore, studies have found assessments of disease activity by patients and physicians are often discordant (Neville et al., 2000) and the SLEDAI is generally not responsive to changes in patients’ assessments of changes in disease activity (Chang, Abrahamowicz, Ferland, & Fortin, 2002). Thus, it seems possible that patients’ psychological adjustment to illness may depend more heavily upon subjective assessments of disease activity, which may not be associated with other measures of disease activity.

The importance of interpersonal relationships in the maintenance of health has been widely reported. Poor social support is expected to increase the burden of illness experienced by the individual. DeVellis and colleagues (1986) reported less-supportive

atmospheres play a role in the onset and exacerbation of autoimmune diseases. In the current study, the hypothesis that response profiles reflecting higher levels of pain, fatigue, and distress would be inversely associated with levels of perceived social support was supported. This finding is consistent with a large body of literature across numerous disease populations reporting that greater social support serves as a buffer against the harmful effects of illness on psychological well-being.

This study provided an interesting approach to grouping patients into psychological response profiles. One of the objectives of cluster analysis is to reveal relationships among observations that were perhaps not possible using individual observations (Hair, Anderson, Tatham, & Black, 1998). This did not appear to be the case for the subgroups found in this study. The subgroups did not demonstrate meaningful relationships with expected variables, bringing into question the usefulness of determining subgroups within AD samples.

The identification of patient subgroups is ultimately beneficial to the extent that they can be utilized in the understanding and treatment of individuals in each subgroup. This type of application has proven successful in the chronic pain literature (e.g., Sanders & Brenna, 1993; Swimmer, Robinson, & Geisser, 1992). Further research investigating treatment outcome differences across clusters is necessary to determine the possible benefits of using clustering techniques to identify subgroups of AD and ANA positive patients. The ability to identify patients who are highly distressed and at increased risk for poor outcomes would allow for the implementation of interventions that are more efficiently tailored to meet the individual's needs.

Future studies investigating whether diagnostic groups within a particular cluster (e.g., "High Impact") are more or less amenable to improvements when a targeted

psychological intervention is applied might help to elucidate relationships between disease and illness response. For example, if ANA patients in the “High Impact” cluster showed greater reductions in psychological distress than SLE patients from the same subgroup, one might suspect that high distress compounded by more severe underlying disease processes are less responsive to psychological intervention.

The findings of this study must be considered in the context of several caveats. First, it is necessary to point out that the cluster analysis technique is a data reduction technique based on both objective and subjective considerations on the part of the researcher. Therefore, if another set of variables had been chosen to include in the cluster analysis, the results could have been quite different. Similarly, it is possible that the variables selected to test predictive validity of the clusters were not the most appropriate in terms of their ability to discriminate between variations in psychological responses. For example, it is possible that the SLEDAI is not an accurate measure of disease activity or that it is not comprehensive and does not adequately capture the component of disease activity associated with symptom (i.e., pain and fatigue) intensity.

An additional caveat relates to the a priori decision to include individuals representing a wide range of diagnostic groups. Although the ANA positive group presents clinically with many of the same complaints as patients who go on to be diagnosed with AD, it is possible that they are a distinct group with regard to response to illness. It is possible that the heterogeneity across the sample diluted the relationship of response profiles to disease-specific measures of function. Thus, future studies attempting to categorize patients based on response profiles might benefit from limiting their sample to a specific diagnostic category before broadening the scope to include multiple diagnoses.

The cross-sectional design on which this study is based limits the exploration of relationships to a single point in time. The temporal relationship between disease activity and psychological functioning remains unclear, although some researchers have suggested that such relationships are not based on a simultaneous pattern of flux. Thus, it is possible that relationships between biological correlates of disease activity and psychological function can only be elucidated when the variables of interest are observed prospectively. Research in the area of relationships between psychosocial and immune parameters would benefit from longitudinal designs to account for temporal relationships that are not revealed within cross-sectional designs.

Finally, the cohort sampled in this study included a relatively small number of men. It remains largely unknown as to whether men responded similarly to the women. These proportions did not allow for tests of gender differences. Future research is needed to better understand psychological response to AD in men and to test for gender differences in symptom reporting and illness response.

Cluster profiles were not validated by demographic, diagnostic, or disease activity measures. Response profiles were related to perceived social support, the only psychosocial variable examined across cluster profiles, suggesting that psychosocial variables function in synchrony. Response to illness in this study was not dependent on disease activity or type, thereby providing greater support for the role of psychological and social support factors in determining response to illness.

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BIOGRAPHICAL SKETCH

Rebecca Jump was born February 25, 1973, as the first of four children. She grew up on the Eastern Shore of Maryland in a small community on the Chesapeake Bay. She graduated from St. Michaels High School in 1991 and headed to the mountains of central Pennsylvania to attend Juniata College. As an undergraduate, she played varsity field hockey and spent one semester in Nancy, France, as part of a study abroad program. She graduated with a Bachelor of Science degree in biopsychology and French in 1995 and promptly headed back across the Atlantic Ocean to further indulge herself in French language and culture. She spent one year in a French language program for foreigners at the Université de Lille III in Villeneuve d'Ascq, France. Upon her return from abroad in 1996, Rebecca began a master's program in the General Experimental Psychology-Health option at the University of Hartford in West Hartford, Connecticut. She spent an additional year in New England working full-time at the University of Connecticut Health Center as a research assistant for parallel studies involving women with fibromyalgia and rheumatoid arthritis. In 2000, Rebecca headed for the sunny south to begin her doctoral training in clinical and health psychology at the University of Florida where she specialized in adult medical psychology with a particular focus on chronic pain and rheumatic disease. In the next phase of her "East Coast Living" Rebecca ventured to Augusta, Georgia, to complete her predoctoral internship at the Medical College of Georgia/Veteran's Affairs Medical Center Training Consortium. During this year of clinical training, Rebecca pursued an advanced specialization in the assessment

and treatment of posttraumatic stress disorder (PTSD). Following the completion of her internship, Rebecca will return to the University of Florida to complete a postdoctoral fellowship in the Department of Clinical and Health Psychology. Her career goal is to obtain a position in a medical center specializing in the treatment of chronic pain/illness and PTSD. She also hopes to devote a portion of her time to research collaboration and supervision of trainees.