Prevalence of Neurocognitive Dysfunction and Other Clinical Manifestations in Disabled Patients with Systemic Lupus Erythematosus

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ABSTRACT. ***Objective***. While work disability is common in patients with systemic lupus erythematosus (SLE), it is not known which lupus disease characteristics predispose toward work disability. We examined demographic, clinical, serological, and neuropsychological factors in a group of disabled and nondisabled patients with SLE.

Methods. Fifty patients meeting American College of Rheumatology criteria for SLE were assessed for work status, disease characteristics, fatigue, anxiety, depressive symptoms, and quality of life. All subjects underwent an abbreviated panel of neuropsychological tests. Subjects who had formal work disability (social security or longterm disability, n = 16) and subjects who self-reported work disability without formal recognition (n = 8) were compared to subjects denying work disability from lupus (n = 26).

Results. Education level, African-American race, and SLICC Damage Index score were significantly associated with formal work disability relative to other subjects. Neurocognitive impairment (OR 14.44, 95% CI 3.01, 68.20; p = 0.001), nephritis (OR 3.75, 95% CI 1.01, 13.9; p = 0.048), and discoid lupus (OR 19.93, 95% CI 3.51, 113.3; p = 0.001) were all associated with formal disability. Formally disabled patients had higher fatigue and anxiety scores and more impaired quality of life in many domains relative to nondisabled subjects. Subjects with self-reported work disability also had neurocognitive dysfunction, high fatigue scores, and poor quality of life, but in other respects appeared to have milder disease than formally disabled subjects.

Conclusion. Neurocognitive dysfunction and fatigue are 2 manifestations that may contribute materially to work disability in lupus. Other associated factors include low education levels, SLICC Damage Index scores, discoid lupus, nephritis, and possibly African-American race. (J Rheumatol 2006; 33:531–8).

Key Indexing Terms:
LUPUS DISABILITY EMPLOYMENT NEUROCOGNITIVE DYSFUNCTION FATIGUE

Systemic lupus erythematosus (SLE) is a chronic and unpredictable disease that often interferes with daily functioning[1]. Many lupus patients will not be able to maintain gainful employment due to their disease[1-4]. Common SLE symptoms such as intermittent fevers, severe fatigue, arthralgias, and serositis are often not detectable or quantifiable on physical examination, nor proven by laboratory or radiographic methods. Thus, many manifestations of SLE that contribute to work disability may not be externally evident.

The study of work disability in SLE is challenging because the study population consists of primarily young and middle-aged women, often during childrearing years. These individuals with lupus may choose to become homemakers or return to the workforce, based on complex decision-making. The severity of their lupus, cultural traditions or expectations, and the financial stability of their family unit all enter into work decisions. Individuals who choose to leave the workforce and become homemakers due to the added stress of their chronic illness will often not be considered in rates of work disability. Thus the true economic and personal impact of SLE on individuals' lives is likely to be underestimated.

One of the most common impairments in SLE is neurocognitive dysfunction, which is estimated to occur in 25%–80% of patients with SLE[5,6]. In multiple sclerosis, neurocognitive dysfunction is a stronger contributor towards work disability than more obvious physical handicaps[7]. However, neurocognitive dysfunction in SLE has been characterized as mild to moderate in degree, and fluctuating over time[8]. These defects are usually nonprogressive[9], although a higher risk of progression has been associated with the presence of antiphospholipid antibodies[10,11]. In contrast to multi-

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ple sclerosis, there is often little evidence for cellular damage in the brain of SLE patients with global neurocognitive dysfunction. Cytokine-induced, reversible neuronal dysfunction has been postulated as a cause, with interleukin 6 (IL-6) felt to be a possible candidate, based on the correlation of IL-6 levels and neurocognitive performance[12]. Another possible mechanism may be autoantibody interference, either by interaction with glutamate receptors[13] or by antiphospholipid antibodies[14] and their binding to neuronal antigens such as myelin[15]. Others[16] have postulated leukothrombosis in the central nervous system, with resultant low-grade ischemia in the absence of clinical stroke syndrome. This view is supported by reports of hypometabolic changes on positron emission tomographic scanning in symptomatic and asymptomatic SLE patients[17]. Nonprogressive, mild, and fluctuating neuronal dysfunction would seem unlikely to cause serious work disability, yet many patients report deterioration in school grades and even interference in activities of daily living related to poor memory and concentration.

We sought to determine the clinical, serological, demographic, and psychological correlates of work disability in lupus, with particular attention to the neurocognitive function of these subjects. By this assessment, we hoped to identify characteristics that increase patients' risk for work disability from lupus. Clinical manifestations, serologies, demographic variables, and neuropsychological functioning were examined in a group of SLE patients of varying employment status. A battery of neuropsychological tests was performed with all subjects. Working SLE patients were compared to patients with formal work disability, and to patients with self-reported inability to work due to lupus.

MATERIALS AND METHODS

Participants. Participants were recruited during routine visits to the outpatient rheumatology clinic at the University of Chicago, predominately from the author's practice (TU), as part of a study examining ethnic/racial variation in neurocognitive function in SLE. Selection of study participants was based on a clinical diagnosis of SLE by a University of Chicago rheumatologist and willingness to participate. Participants did not receive compensation for their participation. The University of Chicago's Institutional Review Board approved the project, and all participants signed informed consent to participation.

Demographic data. Demographic information, including work status, was acquired by a standardized questionnaire administered to all participants. Other demographic data included age, gender, ethnic and racial group, years of education, and duration of SLE.

Work disability status. Subjects were divided into groups based on work disability status. Formal work disability (FD) was defined as the current receipt of longterm disability payments or social security due to lupus. Self-reported work disability (SRWD) was defined as patient report of inability to work due to lupus, but without the formal recognition of disability as defined above. Nondisabled subjects (ND) denied work disability due to lupus.

Clinical characteristics. Disease manifestations (malar rash, discoid rash, photosensitivity, oral ulcers, leukopenia, lymphopenia, thrombocytopenia, arthralgia/arthritis, serositis, nephritis, central nervous system disease excluding neurocognitive dysfunction, and peripheral neurological disease) and Systemic Lupus International Collaborating Clinics Damage Index (SLICC DI) scores[18] were determined by chart review on all patients. Because neurocognitive impairment was a major variable of interest, this item was excluded from overall SLICC DI score. Organ involvement was defined based on the American College of Rheumatology (ACR) criteria for the classification of SLE[19], with the exception of neurological involvement by SLE, which was expanded as described by the ACR Ad Hoc Committee on Neuropsychiatric Lupus[20]. Coexistence of clinically evident Sjögren's syndrome (SS) and fibromyalgia syndrome (FM) in the SLE participants was also determined by chart review. Due to the retrospective nature of the chart review, formal cross-sectional assessment and criteria for the diagnosis of SS and FM were not used.

Laboratory measures were determined by review of charts, and computerized laboratory records dating to 1993. Measures included antinuclear antibody titer (ANA), anti-double stranded deoxyribonucleic acid antibody (dsDNA), Sjögren's syndrome A antibody (SSA), B antibody (SSB), Smith (Sm), anti-ribonucleoprotein (RNP), complement components C3 or C4, anticardiolipin antibody (aCL) IgG or IgM, lupus anticoagulant assay, and anti-$ß_2$-glycoprotein-I (anti-$ß_2$-GPI) IgG, IgM, or IgA. ANA was performed by immunofluorescence on HEp-2 cells. ANA titers of 1:80 or higher on any occasion were considered positive. The presence of dsDNA antibodies was determined by the Crithidia method (Immunoconcepts, Sacramento, CA, USA), and a titer of 1:10 or higher at any time was considered positive. ELISA assays (Inova Diagnostics, San Diego, CA, USA) were used to determine RNP, Sm, SSA/SSB, aCL IgG and IgM, anti-$ß_2$-GPI IgG, IgM, or IgA; and abnormalities were based on the routine upper limits of normal for these commercial assays. A lupus anticoagulant assay was considered positive if tissue thromboplastin time or a diluted Russell viper venom time was prolonged, and a confirmatory platelet neutralization test was positive. Hypocomplementemia was defined as present if C3 or C4 were ever observed to be low.

Neuropsychological assessment. Participants completed a neuropsychological test battery administered by a trained psychometrician, which was designed to assess a range of abilities. Measures proposed by the ACR Ad Hoc Committee on Neuropsychiatric Lupus Nomenclature[20] were supplemented with additional measures, which have been standardized and validated in prior studies of both normal and brain damaged individuals[21].

An estimate of premorbid verbal IQ was provided by administration of the National Adult Reading Test–Revised[22]. The California Verbal Learning Test (CVLT)[23] and Rey Complex Figure Test (RCFT)[24] were used to measure verbal and visual memory, respectively. Attention/processing speed measures included the Stroop Color-Word Test (SCWT)[25], Trail Making Test, and both the written and oral versions of the Symbol Digit Modalities Test (SDMT)[26]. Letter-number sequencing from the Wechsler Adult Intelligence Scale, 3rd edition[27], was used to assess working memory. Aspects of language function were measured with the Controlled Oral Word Association Test (FAS) and Animal Naming. Finger tapping from the Halstead-Reitan battery was employed to assess motor speed. Raw scores from the neuropsychological tests were transformed into standardized scores using published normative data for specific tests.

Upon completion of neuropsychological measures, each neurocognitive profile was assigned a qualitative rating, reflecting a neuropsychologist's (ND) global judgment as to the presence of cognitive impairment evident across measures. This neurocognitive performance severity scale, consisting of a 9-point ordinal scale ranging from 1 (above average) to 9 (severe impairment), was adapted based on previous evidence supporting the validity and reliability of such procedures to rate clinical neuropsychological impairment among numerous neurological disorders[28,29]. Individuals with a rating of either 1 (above average), 2 (average), or 3 (low average) were designated unimpaired, whereas individuals with a qualitative rating $\geq$ 4 were designated as impaired. Since many healthy individuals exhibit isolated impairments in single neuropsychological test performance[30], participants had to exhibit impaired performance on measures in at least 2 specific ability areas in order to receive a global rating in the impaired range (rating > 4: neurocognitive impairment).

Current self-reported pain levels were measured using the Short-Form McGill Pain Questionnaire (SF-MPQ)[31]. Research has validated the sensory, affective, and total scores of the SF-MPQ among individuals with chronic pain due to cancer[32].

Psychological functioning was assessed in regard to trait anxiety, depressive symptoms, and fatigue. The State-Trait Anxiety Inventory (STAI)[33] and Center for Epidemiologic Studies Depression Scale (CES-D) were used for the assessment of emotional status. Raw scores from the STAI were converted to percentiles referencing published normative databases. The CES-D employs a 4-point rating scale (0/1/2/3) yielding a maximum score of 60, with higher scores indicating greater depressive symptomatology[34]. Fatigue was assessed using the Multidimensional Fatigue Inventory (MFI-20)[35]. Item responses were recorded on a 5-point ordinal scale, with higher scores indicating greater fatigue. Participants also completed a quality of life index, reporting on aspects of physical, mental, and social function. The Short Form Health Survey (MPQ, SF-36) is a 36-item instrument that was constructed to survey health status in a study of medical outcomes[36]. The SF-36 has been used widely to monitor outcomes in lupus clinical research, yielding solid evidence of both construct and convergent validity[37].

Statistical analyses. All analyses were conducted with Stata 8.0 software. Subjects were divided into groups based on work disability status (FD, SRWD, and ND). Fisher's exact test assessed demographic, clinical, and serological correlates of formal and self-reported work disability relative to nondisabled subjects. Multivariate analysis of variance (MANOVA) was used to assess the outcome of the neuropsychological battery in FD and SRWD, versus those denying work disability (ND). Results of the depression index, fatigue inventory, anxiety scales, pain scales, and the domains of the SF-36 were also compared by disability group using t tests.

Subsequently, univariate logistic regression was used to estimate odds ratios (OR) and confidence intervals (CI) for associated demographic, clinical, and psychological results. Significant variables on univariate regression were then used together in multivariate logistic regression to test for independent significance. All analyses were conducted with a 2-tailed type I error level of 0.05.

RESULTS

Fifty-three participants with the clinical diagnosis of SLE agreed to participate in neuropsychological testing from 2000 to 2003. From this larger sample, 50 fulfilled revised criteria for SLE as outlined by the ACR[19] and were retained for further analyses. Sixteen subjects were formally disabled, 8 self-reported work disability in the absence of formal disability status, and 26 denied work disability. A summary of demographic, clinical, and serological data for the study population is provided in Table 1. The sample was predominantly female (92%), with ethnic minorities highly represented. Sixty percent (n = 30) of the sample was African-American, whereas the remainder consisted of Caucasian (n = 13), Hispanic (n = 5), or Asian-American (n = 2) individuals. The mean age of participants at the time of neuropsychological testing was 41 years (SD 11.53) with a mean length of illness averaging less than a decade (8.58 yrs, SD 8.32). Educational attainment was somewhat above the equivalent of a high school diploma (13.82 yrs, SD 2.47). The mean SLICC DI score was 2.32 (SD 2.6), with a median score of 2.0. Thirty percent of the SLE participants were noted to have concurrent SS, while only 6% had concurrent FM noted on chart review. Because so few patients had FM noted on chart review, this variable was dropped from further analysis.

Neurocognitive functioning. Fifty percent of the overall cohort had neurocognitive impairment. Because the neurocognitive performance severity scale has not been used in lupus previously, this scoring technique was validated in our study by a blinded review of half the subjects by a second neuropsychologist (JF). The 1–9 (semiquantitative) scale had excellent agreement by Pearson correlation (0.74, $p < 0.001$), but the weighted kappa score was quite low at 0.43. Thus, neurocognitive performance was summarized into a dichotomous rating of normal (scores of 1–3) versus impaired (scores of 4–9). With this dichotomous (qualitative) rating system, the agreement was substantial with a kappa = 0.66. The dichotomous rating system was then used in all further analyses.

Table 1. Demographic and clinical characteristics of study group. Values are percentages unless otherwise indicated.

Mean age, yrs (SD)	41.0 (11.5)
Male/female ratio	4/46
Race	
African-American	60
Caucasian	26
Other	14
Mean SLE Duration, yrs (SD)	8.6 (8.3)
Mean education level, yrs (SD)	13.8 (2.5)
SLICC score, median (mean, SD)	2.00 (2.32, 2.6)
Malar rash	44
Discoid rash	22
Arthralgia/arthritis	94
Serositis	44
Nephritis	42
Neuropsychiatric SLE*	38
Neurocognitive dysfunction	50
dsDNA antibodies (N = 49)	60
Sm (N = 46)	21
RNP (N = 46)	46
SSA antibodies (N = 41)	39
SSB antibodies (N = 41)	3
Thrombocytopenia (N = 49)	16
Leukopenia (N = 49)	58
Anticardiolipin IgG (N = 44)	24
Anticardiolipin IgM (N = 44)	20
Lupus anticoagulant (N = 38)	12
Hypocomplementemia (N = 49)	70
Concurrent Sjögren's syndrome	30
Concurrent fibromyalgia	6

SD: standard deviation, (N =): number of study subjects out of 50 with this serological data available for analysis. * Neuropsychiatic lupus excluding neurocognitive dysfunction.

Formally disabled subgroup. Sixteen patients had formal work disability. Demographic, clinical, and serological characteristics of this group are summarized in Table 2. There were no differences between the FD and ND groups with respect to age. Disease duration was 11.6 (SD 8.8) in the FD group, and 8.23 (SD 8.6) in the ND group ($p = 0.051$). Ethnicity/race was nonrandomly distributed, with an excess of formal disability in African-American subjects with FD relative to ND by Fisher's exact test ($p = 0.023$). Individuals who received formal disability benefits completed fewer years of formal education than individuals who denied work disability ($p = 0.01$). Damage was greater in the FD group, with formally disabled subjects having a mean SLICC DI of 3.8 (median 3.0, SD 2.2) versus nondisabled subjects with a mean SLICC

Table 2. Demographic and clinical characteristics by disability status. Values are percentages unless otherwise indicated.

	Formal Work Disability (FD), n = 16	Self-Reported Work Disability (SRWD), n = 8	Nondisabled (ND), n = 26	p value (FD vs ND)	p value (SRWD vs FD)
Age, mean (SD)	44.8 (11.1)	35.6 (11.2)	40.3 (11.5)		
Race					
African-American (AA)	87.5	50	46.1	0.010†	
Caucasian	6.2	25	38.5		
Other	6.2	25	15.4		
SLE duration, yrs, mean (SD)	11.6 (8.9)	4.0 (3.2)	8.23 (8.6)		0.008
Education level, yrs, mean (SD)	12.8 (2.2)	13.2 (2.0)	14.6 (2.5)	0.01	
SLCC score median (mean, SD)	3.0 (3.8, 2.3)	2.0 (1.9, 1.6)	1.0 (1.2, 1.4)	< 0.001	0.047
Malar rash	43.8	50	44.0		
Discoid rash	56.2	0	8.3	< 0.001	
Nephritis	62.5	37.5	30.8	0.044	
Neuropsychiatric SLE*	56.2	37.5	26.9	0.066	
Neurocognitive dysfunction**	81.2	75	23.1	< 0.001	
dsDNA antibodies	50.0	62.5	72		
Hypocomplementemia	75.0	50	76		
SSA antibody	57.1	28.6	30.0		
Anticardiolipin IgG	46.7	14.3	18.2		
Sjögren's syndrome	43.8	12.5	26.9		

SD: standard deviation. p values not indicated are > 0.05. * Neuropsychiatic SLE excluding neurocognitive dysfunction. ** Neurocognitive Severity Score ≥ 4. † p value AA race vs non-AA race.

DI score of 1.2 (median 1.0, SD 1.4; p = 0.0007). Coexistence of clinically evident SS was not associated with receipt of formal disability benefits, although it trended toward greater prevalence in the FD group.

Clinical manifestations of SLE associated with formal work disability included discoid lesions (p < 0.001), nephritis (p = 0.044), and neurocognitive impairment (p = 0.002). Neuropsychiatric SLE (excluding neurocognitive impairment) trended toward an association with formal work disability (p = 0.066). There was a trend towards greater frequency of both aCL IgG and SSA antibody among subjects with formal work disability (p = 0.071 and 0.085, respectively). Because many comparisons were included in this analysis, these trending associations may not be significant. Other antiphospholipid assays, anti-dsDNA antibodies, Sm antibody, and hypocomplementemia were not associated with work status.

The neurocognitive performance of formally work disabled subjects was compared to subjects denying work disability in the domains of verbal memory (CVLT), verbal fluency (animal naming and FAS), visual memory (RCFT), attention and processing speed (SCWT, trails tests, and SDMT), working memory (letter-number sequencing), and motor speed (finger tapping tests) by MANOVA. Verbal memory, verbal fluency, and motor speed did not differ between these groups, but visual memory by RCFT (p = 0.0097), and the measures of processing speed and attention (trails tests p = 0.012, SCWT p = 0.013, SDMT p = 0.008) were significantly worse in the group with formal work disability.

Additional analyses were conducted to assess for potential between-group differences with respect to measures of pain, fatigue, depression, anxiety, and health status (Table 3). Anxiety levels were worse in the FD group relative to ND (p = 0.02), while depressive symptoms and pain did not differ between these groups. Fatigue scores were significantly worse in the disabled group (p = 0.03). The FD group endorsed worse health status on the SF-36 domains of physical function (p = 0.0054), general health (p = 0.0144), mental health (p = 0.0155), and the physical function composite score (p = 0.0168) relative to the nondisabled group.

Odds ratios of formal work disability, estimated by univariate logistic regression, were significant for a number of characteristics (Table 4). Higher education yielded an OR of 0.70 (95% CI 0.52, 0.96, p = 0.026) per year of education for formal work disability. Thus greater educational achievement made formal work disability less likely. African-American race was associated with an OR of 8.17 (95% CI 1.54, 43.39, p = 0.014) for formal work disability. Thus African-American subjects were about 8 times as likely to have formal work disability relative to non-African-American subjects. SLICC DI scores also yielded significant OR. Each increment of 1 unit on the SLICC DI score increased the likelihood of formal work disability on average by 2.32 (95% CI 1.33, 4.05, p = 0.003). The presence of neurocognitive impairment increased the odds of formal work disability by 14.44 (95% CI 3.01, 68.20, p = 0.001). OR for formal work disability given nephritis or discoid lupus were 3.75 (95% CI 1.01, 13.9, p = 0.048) and 14.79 (95% CI 2.57, 85.11, p = 0.003), respectively.

Multivariate logistic regression was then performed in order to examine the joint effects of disease duration, race, education level, total SLICC DI scores, neurocognitive dysfunction, nephritis, discoid lupus, and fatigue on disability status. The model was initially selected by backward elimination.

Table 3. Mean (standard deviations) of psychological and quality of life scales, by disability status. Values are mean (SD).

	Formal Disability (FD)	Self-Reported Work Disability (SRWD)	No Disability (ND)	p value (FD vs ND)	p value (SRWD vs ND)
Depression (CES-D)	22.5 (10.8)	25.4 (13.8)	16.7 (12.7)	NS	NS
Trait anxiety (STAI)	63.4 (12.3)	64.1 (10.2)	54.8 (12.0)	0.020	NS
Sensory pain (MPQ-S)	5.5 (5.4)	9.5 (6.9)	5.6 (6.6)	NS	NS
Affective pain (MPQ-A)	2.6 (2.4)	3.5 (3.3)	1.6 (2.0)	NS	NS
Fatigue (MFI)	45.6 (15.2)	62.1 (11.2)	33.8 (14.9)	0.03	0.0001
SF-36 domains (selected)					
Physical function	33.2 (8.8)	26.3 (7.8)	42.7 (11.4)	0.0054	0.0005
Role physical	36.5 (12.6)	31.0 (5.5)	42.1 (12.4)	NS	0.0331
General health	32.3 (9.6)	30.1 (7.4)	39.2 (7.7)	0.0144	0.0158
Mental health	37.1 (12.2)	38.8 (18.8)	47.38 (10.8)	0.0155	NS
Physical composite	32.7 (6.7)	27.0 (8.8)	40.6 (11.1)	0.0168	0.0019
Mental composite	41.9 (12.4)	37.0 (16.8)	47.3 (12.8)	NS	NS

NS: nonsignificant.

Only neurocognitive impairment (p = 0.006) and SLICC DI score (p = 0.005) remained independently predictive of formal work disability. Expanding the model by reentering the removed variables suggested a trend toward association of African-American race (p = 0.063) and discoid rash (p = 0.051) with formal work disability, after adjusting for neurocognitive impairment and SLICC DI score. However, due to the small sample size, the final multivariate model did not provide very good fit. Because SLICC DI scores are cumulative scores of damage in various organs, the logistic regression was repeated excluding SLICC DI, while including specific disease manifestations such as nephritis and other neuropsychiatric lupus. However, no new significant organs were identified in the absence of the SLICC DI variable.

Self-reported work disability. Further sets of analyses were conducted to compare the 8 individuals who self-report disability but do not receive formal disability benefits (SRWD) with individuals receiving disability benefits and nondisabled individuals. Because this is a very small group, analyses were limited. Of the 8 patients, 4 were African-American, 2 Caucasian, and 2 Hispanic. Mean SLE duration was shorter than in the formal disability group (4.0 yrs, SD 3.15, p = 0.008). ND subjects were more likely to have education levels beyond high school graduation than SRWD subjects (p = 0.048). Thus the SRWD group had short disease duration and relatively less education. Seventy-five percent of the subjects in this group had neurocognitive impairment, compared to 81% in the FD group and 23% in the ND group (p = 0.014, SRWD vs ND). In contrast, the frequency of nephritis, discoid lupus, and SLCC DI scores in the SRWD group did not significantly differ from the nondisabled group. The FD group had significantly higher SLICC DI scores than the 8 individuals in the SRWD group (p = 0.047; Table 2).

There was a trend toward greater depressive symptoms, trait anxiety, and pain in this small group relative to ND, which did not reach statistical significance. Fatigue scores in the SRWD were markedly elevated relative to the ND group (Table 3; p = 0.0001). Individuals claiming work disability without formal disability status had markedly impaired functioning across many domains of the SF-36. The SRWD group endorsed worse physical function (p = 0.0005), general health (p = 0.0158), vitality (0.0088), and composite physical function (0.0019), but did not differ on mental health or mental composite scores relative to the ND group. Overall, their SF-36 scores were equal to or worse than seen in the FD.

DISCUSSION

The population in this study is relatively unique in respect to its large number of African-American subjects (60%) and quite high SLICC DI scores relative to other studies in SLE[38,39], indicating some increased severity of disease. However, in other respects such as duration of disease, age, and disease manifestations (Table 1), this group resembles other multiethnic SLE populations[40,41]. Because the study's primary focus was on neurocognitive function, patients with neurocognitive complaints may have been more likely to agree to the study. Thus our sample of SLE patients may be enriched in neurocognitive impairment relative to our whole SLE population due to effects of self-selection, although our 50% frequency of neurocognitive impairment is within the ranges reported in previous studies[5,6].

In our cohort, 32% of subjects had obtained formal disability status, 16% self-reported work disability but did not have formal disability status, and 52% denied work disability due to lupus. Lower education level and African-American race, but not age or disease duration, were associated with a greater likelihood of formal work disability. Clinical manifestations of discoid lupus, lupus nephritis, neurocognitive dysfunction, and overall SLICC DI score were significantly increased in the FD group. While neurocognitive dysfunction and discoid lupus were highly associated with formal disability, lupus nephritis just barely reached statistical significance. Concurrent SS and neuropsychiatric SLE (excluding neurocognitive dysfunction) trended toward an association with

FD. No serological manifestations were significantly different between groups (Table 2). Subjects with formal work disability had significantly worse anxiety levels and fatigue compared to working subjects. Quality of life was worse in multiple domains in the FD group, consistent with more severe disease. Depressive symptoms did not differ significantly between groups (Table 3).

Multivariate logistic regression with demographic and clinical variables eliminated education level, discoid lupus, nephritis, and fatigue levels from significance, leaving only neurocognitive dysfunction and SLICC DI scores significantly associated with formal work disability.

As in many lupus studies, assessment of effects of African-American race may be confounded by socioeconomic status. However, education level was similar between African-American (13.53 yrs, SD 2.48) and Caucasian subjects (14.64 yrs, SD 2.31; $p > 0.05$). As a post hoc analysis, due to concern about confounding between socioeconomic status and race, assessment of insurance type among racial groups was attempted. Insurance type was available on 26 of 50 subjects. Within this subset of 26 subjects, Medicaid insurance was significantly associated with African-American status by chi-square testing ($p = 0.013$), supporting a potentially lower socioeconomic status in this group. Individuals of lower socioeconomic status are significantly more likely to be disabled by chronic disease than those of higher socioeconomic status[42,43]. However, Andresen and Brownson[44] identified increased work disability rates in minority women among the general population of the United States, which persisted after adjustment for socioeconomic status. Thus, work disability may be more common among our African-American subjects due to disease character, lower socioeconomic status, or other undefined societal factors.

The association of discoid lupus and lupus nephritis with formal disability status may reflect the effect of externally measurable disease on the ability to obtain formal recognition of chronic illness. Nephritis is easily quantifiable based on renal function tests and levels of proteinuria. Discoid lupus is a chronic, visible, and disfiguring rash, which, in addition to being objectively observable to a disability assessor, may also result in impairment of social function due to disfigurement. The correlation of work disability with SLICC DI score, as a summary measure of damage in lupus, is not surprising and adds face validity to our findings.

Self-reported work disability was present in 8 patients. These patients tended to be younger, have shorter disease duration, and have low SLICC DI scores relative to formally disabled patients. Clinical markers most resembled the nondisabled group, with the exception of neurocognitive dysfunction, which was present in 75% of SRWD subjects. Fatigue levels were much higher in SRWD subjects, while depressive symptoms, anxiety, and pain all trended higher in this group. Physical function, general health, and vitality scores in this group were similar to or worse than those seen in the FD group. Poor neurocognitive function in this group might relate to psychological distress, fatigue, or to their relatively new-onset lupus. Because our number of subjects in this interesting group is small, no definite conclusions about its characteristics can be drawn.

Our findings of 36% of SLE subjects on formal disability and 48% overall not working due to lupus are fairly congruent with previous studies reporting employment rates in SLE[1-3]. Partridge, *et al*[46] examined risk factors for early work disability in SLE. In a cohort with an average of 3.4 years' disease duration, 68% reported some change in job status due to lupus. Forty percent had stopped work completely. Risk of work disability in this early lupus population was not associated with race, sex, disease duration, SLICC DI score, working status at diagnosis, or occupational prestige. Measures of low socioeconomic status, including low education levels, lack of private insurance, poverty level incomes prior to work disability, and jobs requiring greater physical strength were all associated with an increased risk for work disability in SLE. Sutcliffe, *et al*[2] found similar associations of lower education levels with increased risk of work disability in SLE.

Our findings suggest that neurocognitive impairment may be a significant contributor to work disability in SLE. However, there are limitations in this study. Because this is a cross-sectional study, we cannot claim a causal relationship between neurocognitive dysfunction and work disability. The labor-intensive nature of formal neuropsychological evaluation limited the size of this study, and thus we may not have had adequate power to detect other important contributors to work disability. Measures of testing effort were not performed on the neurocognitive assessment, leaving open the possibility of poor effort due to fatigue or other factors. However, fatigue scores did not reduce the association of work disability with neurocognitive performance on multivariate logistic regression. FM was not assessed because it appeared to be underreported on chart review, appearing in only 6% of subject charts. However, the lack of association of pain and depression scores with work disability suggests that concurrent FM is not driving these results. A larger lupus cohort will need to be examined longitudinally to define the contribution toward work disability of non-neurocognitive factors, and to define the temporal relationship between work disability and neurocognitive decline.

Our finding of substantially increased prevalence of work disability in the presence of neurocognitive dysfunction suggests that this impairment may have a high impact on the daily functioning of SLE patients. Fatigue and global neurocognitive complaints are nonspecific, nonobjective disease features that are likely to be discounted by disability assessors. Comprehensive neuropsychological testing is also not routinely done as a part of work capacity assessment in lupus patients. It may be appropriate to perform neuropsychological assessments and standardized fatigue instruments on SLE patients who find themselves unable to work. The develop-

ment of short computerized batteries to longitudinally track neurocognitive function may make this assessment practical in clinical settings[47]. These assessments may serve as objective measures of common neurocognitive impairments in patients with SLE. In turn, obtaining formal recognition of work disability for impaired lupus patients may improve their access to medical care, a significant determinant in disease outcome[48,49].

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