Published in final edited form as:
Arthritis Care Res (Hoboken). 2012 April ; 64(4): 502–510. doi:10.1002/acr.21587.

Physical activity, obesity, and cognitive impairment among women with systemic lupus erythematosus

Patricia Katz, PhD, **Laura Julian, PhD**, **Mary C. Tonner, MA**, **Jinoos Yazdany, MD, MPH**, **Laura Trupin, MP**, **Edward Yelin, PhD**, and **Lindsey A. Criswell, MD, MPH**
University of California, San Francisco

Abstract

Objective—Examine relationships of obesity and physical inactivity to cognitive impairment in women with systemic lupus erythematosus (SLE).

Methods—Body composition was measured with dual-energy x-ray absorptiometry (DXA) for 138 women with SLE. Obesity was defined by total % body fat. Physical activity was ascertained with the self-reported International Physical Activity Questionnaire (IPAQ); inactivity was defined as expenditure of ≤600 metabolic equivalent (MET) minutes/week. Cognitive function was assessed with a 12-index neuropsychological battery. Impairment was defined as age-adjusted z-scores ≤1.5 SDs below mean on 1/3 of tests completed. Scores were obtained for the total battery and for memory and executive function components. Multivariate analyses examined the relationship of obesity and physical activity, individually and combined, with cognitive impairment, controlling for education, race/ethnicity, disease activity, glucocorticoid use, and depression.

Results—20% of subjects were cognitively impaired, 28% physically inactive, and 50% obese. 5% of active women were impaired on the executive function battery, compared to 23% of those who were inactive (p=0.003). Obese women were more likely to be impaired on the total battery (6% vs. 23%, p=0.007) and on the executive function portion (2% vs. 19%) than non-obese women. In multivariate analysis, both inactivity and DXA-defined obesity were significantly associated with impairment in executive function (Inactivity: OR=9.4 [1.7, 52.8]; Obesity: OR=14.8 [1.4, 151.0]).

Conclusion—Both obesity and inactivity were significantly and independently associated with impairment in cognitive function. If longitudinal studies show that physical inactivity and obesity are precursors to cognitive impairment, these may become important targets for intervention.

Cognitive dysfunction is common in systemic lupus erythematosus (SLE), with prevalence rates ranging from 20–80%, largely depending on methodological and diagnostic practices(1–5). The nature of the cognitive deficits common in SLE include difficulties in the domains of verbal and visual learning and memory, attention, concentration, visual-spatial functioning, and executive functioning(3, 6–8), yet the mechanisms leading to cognitive impairment are not well understood(9).

In the general population, there is increasing appreciation of the role of physical inactivity and obesity as important determinants of cognitive decline. A number of large-scale studies have observed relationships among low levels of physical activity and lower kilocalorie expenditures as predictors of cognitive dysfunction and longitudinal decline in cognitive function(10–12). Similarly, relationships have been observed between metrics of obesity and

Corresponding author: Patricia Katz, PhD, University of California, San Francisco, 3333 California Street, Suite 270, San Francisco, California 94143-0920, Phone: 415-476-5971, Fax: 415-476-9030, patti.katz@ucsf.edu.

accelerated cognitive decline(13, 14). Further, there is increasing evidence that interventions targeting improved cardiorespiratory fitness and decreasing adiposity may buffer against cognitive decline(15).

While rates of obesity and physical inactivity appear to be elevated in SLE(16–23), neither of these factors has been examined in relation to cognitive impairment in SLE. Thus, the objective of this analysis was to examine the relationship of both obesity and physical activity to cognitive impairment in women with SLE.

Methods

Subjects

The sample for the present study was drawn from participants in the UCSF Lupus Outcomes Study (LOS). Participants in the LOS had formerly participated in a study of genetic risk factors for SLE outcomes (24, 25); were recruited from both clinical and community-based sources, including UCSF-affiliated clinics (22%), non-UCSF rheumatology offices (11%), lupus support groups and conferences (26%), and newsletters, websites and other forms of publicity (41%); and participate in annual structured telephone interviews. SLE diagnoses using American College of Rheumatology criteria(26) were verified by medical record review. Additional details regarding the LOS are reported by Yelin et al (27). LOS participants who lived in the greater San Francisco Bay Area were recruited for an in-person assessment in the UCSF Clinical and Translational Science Institute's Clinical Research Center (CRC) that included measurement of body composition and cognitive function. Exclusion criteria were non-English-speaking, younger than age 18, current daily oral prednisone dose of 50 mg or greater, current pregnancy, uncorrected vision problems that would interfere with reading ability, and joint replacement within one year.

325 individuals appeared to be eligible for the CRC study and were asked to participate during one of their annual telephone interviews; 74 (22.8%) were ineligible (35 were actually outside the recruitment area, 25 were too ill, 9 had had recent surgery, 2 were pregnant, 2 had poor English skills, and 1 had severe cognitive problems and was unable to complete the telephone interview). Of the 251 eligible individuals, 84 (33.5%) declined participation. The most common reasons for declining were primarily related to transportation (n = 12) and scheduling difficulties (n = 39). 163 individuals completed study visits. Fifteen participants were excluded from analysis because they did not complete either the cognitive testing or the body composition assessment. Of the remaining 148, 138 were women and were included in these analyses. (The 10 men were excluded because of known gender differences in body composition, and there were too few men for separate analysis.) Sociodemographic and health-related characteristics of the study sample are shown in Table 1.

The study was approved by the UCSF Committee on Human Research.

Measures

Cognitive function

To determine the presence of neuropsychological impairment, a battery of 12 tests was modified from the ACR recommended one-hour battery for SLE, which has been previously determined to be reliable and valid in SLE(28, 29). The battery was divided into two broad indices of cognitive functioning, memory and executive functioning.

The verbal and nonverbal episodic memory index included the following 6 tests:

- California Verbal Learning Test - II (CVLT-II) Learning Trials 1 through 5, Short Delay Free Recall, and Long Delay Free Recall(30); and
- Rey Complex Figure Test Copy Trial, Immediate Delay, and Long Delay(31, 32).

Executive functioning broadly includes higher order cognitive functions including such domains as problem solving, behavioral inhibition, organization, task set-shifting, reasoning, sequencing and planning. The executive functioning index was comprised of the following 6 tests:

- Controlled Oral Word Association Test (COWAT) total correct on phonemic fluency (letters)(33);
- Delis-Kaplan Executive Function Test (DKEFS) Design Fluency Test – Shifting condition(34);
- DKEFS Color Word Inhibition Test – Inhibition Condition(34);
- DKEFS Color Word Inhibition Test – Switching condition(34);
- DKEFS Card Sorting Test – Total Correct sorts (Set 1)(34); and
- DKEFS Trail Making Test – Shifting Condition(34).

For each index, impairment was assigned if performance fell below −1.5 SD of age-adjusted population normative data. Using a conventional approach, patients were classified as having neuropsychological impairment if they were impaired on at least one third of the indices in each battery (total, memory, executive function)(29). Women could be considered impaired on the total battery or on either the memory or executive function Indices alone. It was possible for women to be impaired on either the memory or executive function index (e.g., impaired on 2 of the 6 memory tests), and not be impaired on the total battery (e.g., impairment on fewer than 4 of the total 12 tests).

Physical activity

Physical activity was assessed by self-report with the long form of the International Physical Activity Questionnaire (IPAQ;(35, 36)). The IPAQ assesses physical activity across four domains: leisure time physical activity, domestic and yard activities, work-related physical activity, and transport-related physical activity. It has been used and validated in a number of populations(36–38). Scoring the IPAQ yields an estimate of energy expenditure in the past week. The scoring protocol provides cut-point by which individuals' energy expenditure can be categorized as low, moderate, or high. Individuals who expended fewer than 600 metabolic equivalent (MET) minutes per week, the definition for low physical activity, were classified as inactive for these analyses(35, 36). To simplify reporting, individuals who reported more than 600 MET minutes per week will be referred to as "active."

Body composition

A Lunar Prodigy™ Dual Energy X-ray Absorptiometry (DXA) scan was performed to assess body composition. The DXA provides good estimates of the amount of body fat and muscle, and has previously been successfully used to assess body composition among individuals with SLE(19, 20, 39) and RA(40–43), and in studies of aging(44–46). DXA results provide a measure of total percent body fat, as well as regional distribution of fat and lean tissue. To define obesity from total % body fat, we used the definitions suggested by Gallagher (47). These definitions are calculated separately for sex, age, and race groups. Body fat percentage criteria for obesity according to these definitions range from 38% for African American women aged 20–39, to 43% for white women aged 60–79(47).

In addition to DXA assessments of body composition, for secondary analyses, we also examined anthropometric measures of body composition because these measures can be more easily implemented in a clinical setting. We collected anthropometric measures often used as proxies of body composition: height and weight, to calculate body mass index (BMI), and waist circumference. Height was measured with a wall-mounted stadiometer. Weight was measured with subjects wearing light indoor clothing and no shoes. BMI was calculated as weight (Kg) divided by height (meters^2). Obesity was defined from BMI using two criteria. The first criterion was BMI≥30 kg/m^2, the common BMI criterion for obesity(48). The second criterion was BMI≥26.8 kg/m^2, a revised obesity criterion recently proposed for women with SLE based on data regarding body composition from DXA analyses of a subset of these women(19). This revised criterion was found to correspond with DXA-defined obesity better than a BMI of ≥30 kg/m^2. Waist circumference was measured at the mid-point between the lower border of the ribs and the iliac crest. Two measurements were taken, and the average measure used. Again, two criteria were used to define obesity. The first was waist circumference ≥88 cm., the common criterion for obesity(48). The second was waist circumference ≥84.5 cm., based on the correspondence of this measurement with DXA-defined obesity(19).

Other variables

Socio-demographic characteristics (age, race/ethnicity, education) were obtained from the baseline LOS telephone interview. Disease activity was assessed using the Systemic Lupus Activity Questionnaire (SLAQ) a validated, self-report measure of disease activity in SLE (49, 50). Current oral glucocorticoid use and dosage was obtained by self-report. The presence of major depressive disorder or any mood disorder was obtained from the M.I.N.I. International Neuropsychiatric Interview (MINI), a brief structured interview for major Axis I psychiatric disorders in DSM-IV and ICD-10 that has high validation and reliability scores. Interviewers were trained and supervised by a licensed psychologist (LJ)(51, 52). In addition, we examined cardiovascular risk using the Framingham cardiovascular disease risk scores (53) and self-reported history of stroke and neurological disorders.

Analysis

Bivariate differences in cognitive impairment were compared between women who were and were not physically inactive and were and were not obese using chi-square analyses. Multivariate logistic regression analyses were conducted to examine the independent contributions of physical inactivity and body composition to impairment on the total cognitive battery and on the memory and executive function components, adjusting for education, race/ethnicity, disease activity using the SLAQ score, glucocorticoid use, and depression. (Norms for calculating z-scores for cognitive tests were age-adjusted, so age was not included in multivariate analyses.) In Step 1 of the logistic regression analyses, models included inactivity only or obesity only, plus covariates (education, race/ethnicity, disease activity, oral glucocorticoid use, and depression). Step 2 of the logistic regression analysis included both inactivity and obesity, plus covariates. Analyses were also conducted examining the interaction of inactivity and obesity (using standard multiplicative interaction terms); no significant interaction effects were found and these analyses are not shown. Because some cell sizes were small (e.g., all but one of the women classified as impaired in executive function was obese), we repeated logistic regression analyses with exact logistic regression. As secondary analyses, we examined anthropometric measures of obesity using the same analysis strategy.

Results

Twenty women (15%) were impaired on the total cognitive battery. There were no significant differences in age, education, duration of SLE, current glucocorticoid use, depression, cardiovascular risk as defined by the Framingham Risk Score, or in self-reported history of stroke or other neurological disorder between women who were and were not impaired on the total battery. Individuals who were impaired were less likely to be white (35% vs. 71.2%, p=.004).

Memory impairment was more common than impairment in executive function (28% compared to 10%). Slightly over one quarter (n = 39, 28%) of the women were physically inactive. Based on total percent body fat from DXA scans (47), 50% (n = 69) were obese.

Using the standard BMI criterion (≥30 kg/m^2), 30% of the women were obese, and 42% were obese using the BMI≥26.8 criterion. Using the standard waist circumference criterion, 41% were obese, whereas 48% were obese using the revised waist circumference criterion.

Bivariate associations with physical inactivity and obesity

On the total cognitive battery, 11% of those who were physically active were impaired, compared to 23% of those who were inactive (p=0.10; Table 2). Forty-one percent of those who were inactive were impaired on the memory component vs. 23% of those who were active (p=0.06), and 5% of those who were active were impaired on the executive function component, compared to 23% of those who were inactive (p=0.003).

Women who were obese by DXA standards were more likely to be impaired on the total battery (23% vs. 6%, p=0.007) and on the executive function portion of the battery (19% vs. 2%, p=.001) than women who were not obese. Obesity was not significantly associated with impairment on the memory battery.

Viewed from a slightly different perspective, of the 20 women who were impaired on the total cognitive battery, 9 (45%) were inactive and 16 (80%) were obese. Among 39 women who were impaired on the memory battery, 16 (41%) were inactive and 24 (62%) were obese; and among 14 women who were impaired in executive function 9 (64%) were inactive and 13 (93%) were obese.

Multivariate associations with physical inactivity and obesity

Controlling for covariates (education, race, SLAQ score, oral glucocorticoid use, and depression), physical inactivity was associated with a significantly elevated risk of age-adjusted impairment in executive function (OR 9.0 [95% CI 1.8, 45.6]) (Table 3, Step 1). The odds of impairment on the total battery and the memory component were elevated, but did not reach statistical significance (Total: OR 2.0 [0.6, 6.3]; Memory: OR 1.9 [0.8, 4.5]; Table 3, Step 1). DXA-defined obesity was associated with both impairment on the total battery (OR 3.4 [1.0, 11.8]) and impairment in executive function (OR 14.3 [1.5, 139.9]), but not with memory impairment.

When physical inactivity and obesity were included in the same model, inactivity remained significantly associated with impairment on the executive function component (OR=9.4 [1.7, 52.8]), but was not associated with impairment on the memory component or the total battery (Table 3, Step 2). Obesity was also independently and significantly associated with impairment in executive function (OR=14.8 [1.4, 151.0]), but not with impairment on the memory component or the total battery.

We repeated analyses using exact logistic regression because the confidence intervals were wide due to the distribution of obesity and impairment. The point estimates obtained from these analyses were lower than those from the original analyses, and although the confidence intervals became wider, the conclusion about statistical significance did not change. For example, the odds ratio from the original logistic regression estimate of DXA obesity on cognitive function was 14.8 (95% 1.4, 151.0); the exact logistic regression odds ratio was 8.3 [95% CI 1.1, 375.4]). It is important to note that one reason for the wide confidence interval was that only one woman with executive impairment was not obese, creating a unbalanced cell in the 2 × 2 distribution (see Table 2).

Secondary analyses using anthropometric measures of obesity

Women who were defined as obese by anthropometric methods had higher rates of impairment on the total cognitive battery, although the difference for the usual BMI definition of obesity (≥30 kg/m^2) was not statistically significant (Table 4). Similar results were found for impairment in executive function. Anthropometric measures of obesity were not significantly associated with impairment on the memory battery.

Controlling for covariates, BMI≥26.8, waist circumference ≥88 cm, and waist circumference ≥84.5 cm were each associated with a higher likelihood of impairment in executive function, although only waist circumference ≥84.5 reached statistical significance (OR 5.5 [1.0, 31.0]; Table 5, Step 1). When both inactivity and obesity were included in the same model, inactivity remained significantly associated with impairment on the executive function component. BMI ≥26.8, waist circumference ≥88 cm, and waist circumference ≥84.5 cm were each associated with a higher likelihood of impairment in executive function, although none of the confidence intervals excluded no relationship (Table 5, Step 2).

Discussion

In this study of women with SLE, both physical inactivity and obesity defined by DXA were significantly associated with impairment in executive function. The findings from this study are comparable to large scale studies in older adults (10, 11). In the general population, decreased physical activity and obesity have each been observed to be associated with executive dysfunction (14, 54, 55). To date, though, these links have been investigated only minimally in rheumatic diseases (56).

Because inactivity and obesity are closely related, it was important to examine the independent contributions of each. When we did so, we found that obesity as defined by DXA and inactivity had independent associations with impaired executive function. Odds ratios for DXA-defined obesity and physical inactivity did not change substantively in the model including both variables, suggesting that inactivity and obesity had independent effects and did not modify the effects of each other.

While obesity defined by DXA was associated with cognitive impairment, obesity defined by BMI and by the standard waist circumference measurement was not associated with impairment after adjusting for covariates. However, waist circumference ≥84.5 cm, a revised obesity criterion defined through our prior work(19), was significantly associated with impairment in executive function. This finding suggests that abdominal fat may be more the critical component of overall body fat, and suggests a simple clinical measure that may identify risk for cognitive impairment.

A variety of mechanistic causes have been proposed for SLE-related cognitive impairment, including both inflammatory and vascular pathways. Inflammatory markers have been linked to cognitive impairment in the general population (21, 57–65). Adipose tissue is a

known source of proinflammatory cytokines, including tumor necrosis factor α (TNF-α and interleukin-6 (IL-6)(66), and regular physical activity appears to decrease levels of inflammatory markers, including c-reactive protein (CRP), IL-6, and TNF-α(67–71). In addition, both sedentary behavior and obesity are established risk factors for cerebrovascular and cardiovascular disease, which, in turn, can influence cognitive dysfunction. Based on our results, future studies evaluating the roles of both inflammatory biomarkers and cardiovascular factors in cognitive decline in SLE appear to be warranted.

This study has limitations that should be considered. First, it is cross-sectional. While our hypothesis is that obesity and physical inactivity may lead to cognitive impairment, it is possible that individuals who are cognitively impaired become less active, and subsequently obese, as a result of their impairment. Mechanisms producing cognitive impairment in SLE are not well defined, so longitudinal studies are needed to try to identify the causal relationships. Although we controlled for disease activity using the SLAQ and current glucocorticoid use, more active or severe disease not accounted for by the SLAQ or long-term glucocorticoid use may result in cognitive impairment or changes in body composition. While we used a well-studied and well-validated measure of physical activity, physical activity was self-reported, and individuals who are impaired may be particularly inaccurate reporters. We do not have data to suggest the direction of a bias in such reporting, if one exists. Women with more severe SLE, and perhaps more importantly, women with more severe cognitive problems, may not have participated because of their inability to travel to the study site or even participate in the telephone interviews, but this differential participation should serve to bias our results toward null findings. In addition, we did not include men in this study. While we have male participants, they are represented at approximately the same rate at which SLE occurs in men (9:1 female:male ratio). This number of men was too small for meaningful analysis, so we cannot generalize results to men with SLE. All of our participants were English-speaking. It is also possible that, while our cohort is composed of 34% racial/ethnic minorities, there are additional racial or ethnic groups to which these results may not be generalizable. Nonetheless, the measure we used to estimate physical activity has been used internationally and validated in a wide variety of languages, and the cognitive function measures have undergone extensive testing and validation. Finally, we caution that our sample size was relative small and some of the estimates lack precision (i.e., had wide confidence intervals). The most obvious example of the lack of precision was the estimate for the odds of impairment in executive function attributable to DXA-defined obesity, due to the finding that all but one individual who exhibited executive dysfunction was obese. Because of this, we encourage future studies to replicate and extend these findings.

Strengths of the study include the comprehensive cognitive function battery that was administered to a large group of women with confirmed SLE. The use of DXA to determine obesity is also a strength, because, as previous noted, BMI is a relatively inaccurate representation of body composition in this group of women with SLE(19).

The results of this analysis may have important clinical implications. Both physical inactivity and obesity are modifiable states. If future longitudinal analyses show that physical inactivity and/or obesity are precursors to cognitive impairment, these may become important targets for intervention to improve cognitive outcomes in SLE.

Acknowledgments

This research was supported by NIH/NIAMS grant P60 AR053308 and by NIH/NCRR UCSF-CTSI Grant Number UL1 RR024131, and by the Rosalind Russell Medical Research Center for Arthritis.

We gratefully acknowledge Sandi Kaplan, BA, Holly Wing, MA, and Rachel Diskin, BS, who conducted the study assessments, as well as Stephanie Rush, BA, who prepared the data for analysis.

References

1. Carbotte R, Denberg S, Denburg J. Prevalence of cognitive impairment in systemic lupus erythematosus. J Nerv Ment Dis. 1986; 174:357–64. [PubMed: 3711879]
2. Hanly J, Fisk J, Sherwood G, Jones E, Jones J, Eastwood B. Cognitive impairment in patients with systemic lupus erythematosus. J Rheumatol. 1992; 19:562–7. [PubMed: 1593578]
3. Kozora E, Thompson L, West S, Kotzin B. Analysis of cognitive and psychological deficits in systemic lupus erythematosus patients without overt central nervous system disease. Arthritis Rheum. 1996; 39:2035–45. [PubMed: 8961909]
4. Sabbadini M, Manfredi F, Bozzolo E, Ferrario L, Rugarli C, Scorza R, Origgi L, Vanoli M, Gambini O, Vanzulli L, Croce D, Campana A, Messa C, Fazio F, Tincani A, Anzola G, Cattaneo R, Padovani A, Gasparotti R, Gerli R, Quartesan R, Piccirilli M, Farsi A, Emmi E, Passaleva A. Central nervous system involvement in systemic lupus erythematosus patients without overt neuropsychiatric manifestations. Lupus. 1999; 8:11–9. [PubMed: 10025594]
5. American College of Rheumatology Ad Hoc Committee on Neuropsychiatric Lupus Nomemclature. The American College of Rheumatology nomenclature and case defintions for neuropsychiatric syndromes. Arthritis Rheum. 1999; 42:599–608. [PubMed: 10211873]
6. Denburg S, Carbotte R, Denburg J. Psychological aspects of systemic lupus erythematosus: Cognitive function, mood, and self-report. J Rheumatol. 1997; 24:998–1003. [PubMed: 9150099]
7. Monastero R, Bettini P, del Zotto E, Cottini E, Tincani A, Balestrieri G, Cattaneo R, Camarda R, Vignolo L, Padovani A. Prevalence and pattern of cognitive impairment in systemic lupus erythematosus patients with and without overt neuropsychiatric manifestations. J Neurol Sci. 2001; 184:33–9. [PubMed: 11231030]
8. Denburg S, Stewart K, Hart L, Denburg J. How “soft” are soft neurological signs? The relationship of subjective neuruopsychiatric complaints to cognitive function in systemic lupus erythematosus. J Rheumatol. 2003; 30:1006–10. [PubMed: 12734896]
9. Kozora E, Hanly JG, Lapteva L, Filley CM. Cognitive dysfunction in systemic lupus erythematosus: Past, present, and future. Arthritis & Rheumatism. 2008; 58(11):3286–98. [PubMed: 18975345]
10. Yaffe K, Barnes D, Nevitt M, Lui L, Covinsky K. A prospective study of physical activity and cognitive decline in elderly women: women who walk. Arch Intern Med. 2001; 161:1703–8. [PubMed: 11485502]
11. Weuve J, Kang J, Manson J, Breteler MMB, Ware J, Grodstein F. Physical activity, including walking, and cognitive function in older women. JAMA: The Journal of the American Medical Association. 2004; 292(12):1454–61. [PubMed: 15383516]
12. Middleton L, Manini T, Simonsick E, Harris T, Barnes D, Tylavsky F, Brach J, Everhart J, Yaffe K. Activity energy expenditure and incident cognitive impairment in older adults. Arch Intern Med. 2011; 171:1251–7. [PubMed: 21771893]
13. Cournot M, Marquié JC, Ansiau D, Martinaud C, Fonds H, Ferrières J, Ruidavets JB. Relation between body mass index and cognitive function in healthy middle-aged men and women. Neurology. 2006; 67(7):1208–14. [PubMed: 17030754]
14. Gunstad J, Paul RH, Cohen RA, Tate DF, Spitznagel MB, Gordon E. Elevated body mass index is associated with executive dysfunction in otherwise healthy adults. Comprehensive Psychiatry. 2007; 48(1):57–61. [PubMed: 17145283]
15. Angevaren M, Aufdemkampe G, Verhaar HJ, Aleman A, Vanhees L. Physical activity and enhanced fitness to improve cognitive function in older people without known cognitive impairment. Cochrane Database Syst Rev. 2008; 3:CD005381. [PubMed: 18646126]
16. Petri M, Perez-Gutthann S, Spence D, Hochberg M. Risk factors for coronary artery disease in patients with systemic lupus erythematosus. Am J Med. 1992; 93:513–9. [PubMed: 1442853]
17. Petri M. Detection of coronary artery disease and the role of traditional risk factors in the Hopkins Lupus Cohort. Lupus. 2000; 9:170–5. [PubMed: 10805483]

18. Bernatsky S, Boivin J, Joseph L, St Pierre Y, Moore A, Rajan R, Clarke A. Prevalence of factors influencing cancer risk in women with lupus: social habits, reproductive issues, and obesity. J Rheumatol. 2002; 29:2251–4. [PubMed: 12415575]
19. Katz P, Gregorich S, Yazdany J, Trupin L, Julian L, Yelin E, Criswell LA. Obesity and its measurement in a community-based sample of women with systemic lupus erythematosus. Arthritis Care Res (Hoboken). 2011; 63(2):261–8. [PubMed: 20824801]
20. Kipen Y, Strauss B, Morand E. Body composition in systemic lupus erythematosus. Br J Rheumatol. 1998; 37:514–9. [PubMed: 9651078]
21. Oeser A, Chung C, Asanuma Y, Avalos I, Stein M. Obesity is an independent contributor to functional capacity and inflammation in systemic lupus erythematosus. Arthritis Rheum. 2005; 52:3651–9. [PubMed: 16258902]
22. Mancuso C, Perna M, Sargent A, Salmon J. Perceptions and measurements of physical activity in patients with systemic lupus erythematosus. Lupus. 2011; 20:231–42. [PubMed: 21183562]
23. dos Santos, FdM; Borges, M.; Correia, M.; Telles, R.; Lanna, C. Assessment of nutritional status and physical activity in systemic lupus erythematosus patients. Rev Bras Reumatol. 2010; 50:631–8. [PubMed: 21243304]
24. Freemer M, King TJ, Criswell L. Association of smoking with dsDNA autoantibody production in systemic lupus erythematosus. Ann Rheum Dis. 2006; 65:581–4. [PubMed: 16150789]
25. Thorburn C, Prokunina-Olsson L, Sterba K, Lum R, Seldin M, Alarcon-Riquelme M, Criswell L. Association of PCDC1 genetic variation with risk and clinical manifestations of systemic lupus erythematosus in a multiethnic cohort. Genes Immun. 2007 Mar 8.10.1038/sj.gene.6364383
26. Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum. 1997; 40(9):1725. [PubMed: 9324032]
27. Yelin E, Trupin L, Katz P, Criswell L, Yazdany J, Gillis J, Panopolis P. Work dynamics among persons with systemic lupus erythematosus. Arthritis Rheum (Arthritis Care Res). 2007; 57:56–63.
28. The American College of Rheumatology nomenclature and case definitions for neuropsychiatric lupus syndromes. Arthritis Rheum. 1999; 42(4):599–608. [PubMed: 10211873]
29. Kozora E, Ellison M, West S. Reliability and validity of the proposed American College of Rheumatology Neuropsychological battery for systemic lupus erythematosus. Arthritis Rheum (Arthritis Care Res). 2004; 51:810–8.
30. Delis, D.; Kramer, J.; Kaplan, E.; Ober, B. Adult Version. 2. San Antonio, TX: Psychological Corporation; 2000. California Verbal Learning Test Manual.
31. Rey, A. L'examen clinique in psychologie. Paris: Presses Universitaires de France; 1964.
32. Corwin J, Bylsma FW. "Psychological examination of traumatic encephalopathy" by A. Rey and "The Complex Figure Copy Test" by P.A. Osterreith. The Clinical Neuropsychologist. 1993; 7:3–21.
33. Spreen, O.; Strauss, E. A compendium of neuropsychological tests: administration, norms, and commentary. 2. New York: Oxford University Press; 1998.
34. Delis, DC.; Kaplan, E.; Kramer, JH.; Ober, BA. Delis-Kaplan Executive Function Scale (D-KEFS). San Antonio: The Psychological Corporation; 2001.
35. Agresti A, Coull B. Approximate is better than "exact" for interval estimation of binomial proportions. The American Statistician. 1998; 52:119–26.
36. Craig C, Marshall A, Sjöström M, Bauman A, Booth M, Ainsworth B, Pratt M, Ekelund U, Yngve A, Sallis J, Oja P. International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc. 2003; 35:1381–95. [PubMed: 12900694]
37. Brown W, Trost S, Bauman A, Mummery K, Owen N. Test-retest reliability of four physical activity measures used in population surveys. J Sci Med Sport. 2004; 7:205–15. [PubMed: 15362316]
38. Hagströmer M, Oja P, Sjöström M. The International Physical Activity Questionnaire (IPAQ): a study of concurrent and construct validity. Public Health Nutr. 2006; 9:755–62. [PubMed: 16925881]

39. Kipen Y, Briganti E, Strauss B, Littlejohn G, Morand E. Three year follow-up of body composition changes in pre-menopausal women with systemic lupus erythematosus. Rheumatology. 1999; 38:59–65. [PubMed: 10334684]
40. Westhovens R, Nijs J, Taelman V, Dequeker J. Body composition in rheumatoid arthritis. Br J Rheumatol. 1997; 36:444–8. [PubMed: 9159537]
41. Rall L, Walsmith J, Snydman L, Reichlin S, Veldhuis J, Kehayias J, Abad L, Lundgren N, Roubenoff R. Cachexia in rheumatoid arthritis is not explained by decreased growth hormone secretion. Arthritis Rheum. 2002; 46:2574–7. [PubMed: 12384914]
42. Roubenoff R, Walsmith J, Lundgren N, Snydman L, Dolnikowski G, Roberts S. Low physical activity reduces total energy expenditure in women with rheumatoid arthritis: implications for dietary intake recommendations. Am J Clin Nutr. 2002; 76:774–9. [PubMed: 12324290]
43. Walsmith J, Abad L, Kehayias J, Roubenoff R. Tumor necrosis factor-α production is associated with less body cell mass in women with rheumatoid arthritis. J Rheumatol. 2004; 31:23–9. [PubMed: 14705214]
44. Visser M, Pahor M, Tylavsky F, Kritchevsky S, Cauley J, Newman A, Blunt B, Harris T. One- and two-year change in body composition as measured by DXA in a population- baesd cohort of older men and women. J Appl Physiol. 2003; 94:2368–74. [PubMed: 12598481]
45. Visser M, Kritchevsky S, Goodpaster B, Newman A, Nevitt M, Stamm E, Harris T. Leg muscle mass and composition in relation to lower extremity performance in men and women aged 70 to 79: the Health, Aging, and Body Composition study. J Am Geriatr Soc. 2002; 50:897–904. [PubMed: 12028178]
46. Visser M, Fuerst T, Lang T, Salamone L, Harris T. Validity of fan-beam dual-energy X-ray absorptiometry for measuring fat-free mass and leg muscle mass. Health, Aging, and Body Composition Study--Dual-Energy X-ray Absorptiometry and Body Composition Working Group. J Appl Physiol. 1999; 87:1513–20. [PubMed: 10517786]
47. Gallagher D, Heymsfield S, Heo M, Jebb S, Murgatroyd P, Sakamoto Y. Healthy percentage body fat ranges: an approach for developing guidelines based on body mass index. Am J Clin Nutr. 2000; 2000:72.
48. World Health Organization. Obesity: preventing and managing the global epidemic. Geneva: World Health Organization; 2000.
49. Karlson E, Daltroy L, Rivest C, Ramsey-Goldman R, Wright E, Patrtridge A, Liang M, Fortin P. Validation of a systemic lupus activity questionnaire (SLAQ) for population studies. Lupus. 2003; 12:280–6. [PubMed: 12729051]
50. Yazdany J, Yelin E, Panopalis P, Trupin L, Julian L, Katz P. Validation of the systemic lupus erythematosus activity questionnaire in a large obsevational cohort. Arthritis Rheum (Arthritis Care Res). 2008; 59:136–43.
51. Sheehan D, Janavs J, Baker K, Harnett-Sheehan K, Knapp E, Sheehan M, Lecrubier Y, Weiller E, Hergueta T, Amorim P, Bonora L, Lepine J. M.I.N.I. Mini International Neurospychiatric Interview. English version 5.0.0. J Clin Psychiatry. 1998; 59 (suppl 20):34–57. [PubMed: 9559758]
52. Sheehan D, Lecrubier Y, Sheehan K, Amorim P, Janavs J, Weiller E, Hergueta T, Baker R, Dunbar G. The Mini-International Neuropsychiatric Interview (M.I.N.I.): The development and validation of a structured diagnostic psychiatric inerview for DSM-IV and ICD-10. J Clin Psychiatry. 1998; 59 (suppl 20):22–33. [PubMed: 9881538]
53. D'Agostino R, Vasan R, Pencina M, Wolf P, Cobain M, Massaro J, Kannel W. General cardiovascular risk profile for use in primary care: the Framingham Heart Study. Circulation. 2008; 117:743–53. [PubMed: 18212285]
54. Bixby W, Spalding T, Haufler A, Deeny S, Mahlow P, Zimmerman J, Hatfield B. The unique relation of physical activity to executive function in older men and women. Med Sci Sports Exerc. 2007; 39:1408–16. [PubMed: 17762375]
55. Eggermont L, Milberg W, Lipsitz L, Scherder E, Leveille S. Physical activity and executive function in aging: the MOBILIZE Boston Study. J Am Geriatr Soc. 2009; 57:1750–6. [PubMed: 19702618]

56. Kozora E, Laudenslager M, Lemieux A, West S. Inflammatory and hormonal measures predict neuropsychological functioning in systemic lupus erythematosus and rheumatoid arthritis patients. J Int Neuropsychol Soc. 2001; 7:745–54. [PubMed: 11575596]
57. Weaver J, Huang M, Albert M, Harris T, Rowe J, Seeman T. Interleukin-6 and risk of cognitive decline: MacArthur studies of successful aging. Neurology. 2002; 59:371–8. [PubMed: 12177370]
58. Yaffe K, Lindquist K, Penninx B, Simonsick W, Pahor M, Kritchevsky S, Slauner L, Kuller L, Rubin S, Harris T. Inflammatory markers and cognitition in well-functioning African-American and white elders. Neurology. 2003; 61:76–80. [PubMed: 12847160]
59. Yaffe K, Kanaya A, Lindquist K, Simonsick E, Harris T, Shorr R, Tylavsky F, Newman A. The metabolic syndrome, inflammation, and risk of cognitive decline. JAMA. 2004; 292:2237–42. [PubMed: 15536110]
60. Gunstad J, Bausserman L, Paul R, Tate D, Hoth K, Poppas A, Jefferson A, Cohen R. C-reactive protein, but not homocysteine, is related to cognitive dysfunction in older adults with cardiovascular disease. J Clin Neurosci. 2006; 13:540–6. [PubMed: 16723232]
61. Rafnsson S, Deary I, Smith F, Whiteman M, Rumley A, Lowe G, Fowkes RF. Cognitive decline and markers of inflammation and hemostatis: the Edinburgh Artery Study. J Am Geriatr Soc. 2007; 55:700–7. [PubMed: 17493189]
62. Gundstad J, Pitznagel SM, Keary T, Glickman E, Alexander T, Karrer J, Stanek K, Reese L, Juvancic-Heltzel J. Serum leptin levels are associated with cognitive function in older adults. Brain Res. 2008; 1230:233–6. [PubMed: 18675793]
63. Hoth K, Haley A, Gunstad J, Paul R, Poppas A, Jefferson A, Tate D, Ono M, Jerskey B, Cohen R. Elevated C-reactive protein is related to cognitive decline in older adults with cardiovascular disease. J Am Geriatr Soc. 2008; 56:1898–903. [PubMed: 18771451]
64. Holden K, Lindquist K, Tylavsky F, Rosano C, Harris T, Yaffe K. Health ABC Study. Serum leptin level and cognition in the elderly: findings from the Health ABC Study. Neurobiol Aging. 2009; 30:1483–9. [PubMed: 18358569]
65. Kamogawa K, Kohara K, Tabara Y, Uetani E, Nagai T, Yamamoto M, Igase M, Miki T. Abdominal fat, adipose-derived hormones and mild cognitive impairment: the J-SHIPP study. Dement Geriatr Cogn Disord. 2010; 30:432–9. [PubMed: 21088422]
66. Coppack S. Pro-inflammatory cytokines and adipose tissue. Proc Nutr Soc. 2001; 60:349–56. [PubMed: 11681809]
67. Geffken D, Cushman M, Burke G, Polak J, Sakkinen P, Tracy R. Association between physical activity and markers of inflammation in a healthy elderly population. Am J Epidemiol. 2001; 153:1286–92.
68. Abramson J, Vaccarino V. Relationship between physical activity and inflammation among apparently healthy middle-aged and older US adults. Arch Intern Med. 2002; 162:1286–92. [PubMed: 12038947]
69. Ford E. Does exercise reduce inflammation? Physical activity and C-reactive protein among US adults. Epidemiol. 2002; 13:561–8.
70. Reuben D, Judd-Hamilton L, Harris T, Seeman T. The associations between physical activity and inflammation markers in high-functioning older persons: MacArthur studies of successful aging. J Am Geriatr Soc. 2003; 51:1125–30. [PubMed: 12890077]
71. Colbert L, Visser M, Simonsick E, Tracy R, Newman A, Kritchevsky S, Pahor M, Taaffe D, Brach J, Rubin S, Harris T. Physical activity, exercise, and inflammatory markers in older adults: findings from the Health, Aging, and Body Composition study. J Am Geriatr Soc. 2004; 52:1098–1104. [PubMed: 15209647]

Significance and innovation

- Cognitive impairment is present in 20–80% of individuals with SLE.
- Obesity and physical inactivity have been linked to cognitive impairment in aging populations.
- Obesity and physical inactivity each appear to be present in a significant portion of individuals with SLE.
- Both obesity and physical inactivity were independently associated with cognitive impairment among this sample of women, and may offer targets for intervention.

Table 1

Sample characteristics (n = 138)

Characteristic	Cognitive function on total battery			
	% (n) or mean (±SD)	Not impaired* (n=118, 85.5%)	Impaired (n=20, 14.5%)	p**
Sociodemographic				
Age, years, mean (SD)	47.8 (±12.5)	47.7 (12.5)	48.6 (13.0)	.76
Race, white, % (n)	65.9 (91)	71.2 (84)	35.0 (7)	.004
Low education†, % (n)	13.0 (18)	11.0 (13)	25.0 (5)	.14
Health-related				
Duration of SLE, years, mean (SD)	15.6 (±9.1)	15.5 (8.7)	15.0 (11.4)	.86
SLAQ score§, mean (SD)	12.6 (±7.5)	12.1 (7.2)	15.4 (8.6)	.07
Current glucocorticoid use				
None	62.3 (86)	61.9 (73)	65.0 (13)	.47
1–4.5 mg/day	5.1 (7)	4.2 (5)	10.0 (2)	
5–9 mg/day	20.3 (28)	22.0 (26)	10.0 (2)	
≥10 mg/day	12.3 (17)	11.9 (14)	15.0 (3)	
Major depressive disorder, % (n)	19.7 (27)	18.6 (22)	26.3 (5)	.53
Framingham Risk Score, mean (SD)	7.8 (5.6)	6.8 (6.6)	8.6 (8.1)	.27
History of stroke, % (n)	6.5 (9)	5.1 (6)	15.0 (3)	.53
History other neurological disorder, % (n)	52.2 (72)	51.7 (61)	55.0 (11)	.81

*Based on total battery

**p-value from t-tests/chi-square analyses comparing impaired vs. not impaired.

†Low education = fewer than 12 years of education

§SLAQ = Systemic Lupus Activity Questionnaire (49, 50). Possible score range 0–44; higher scores reflect greater disease activity.

¶At least 1.5 SD below the mean on 1/3 of measures completed

Table 2

Bivariate analysis: Associations of body composition and physical inactivity with cognitive impairment

		% (n) cognitively impaired		
		Total battery 14.5% (n = 20)	**Memory 28.3% (n = 39)**	**Executive function 10.1% (n = 14)**
Physical activity	Active (n = 99)	11.1% (11)	23.2% (23)	**5.1% (5)**
	Inactive (n = 39)	23.1% (9)	41.0% (16)	**23.1% (9)**
	p*	0.10	.06	**.003**
Obese by DXA (reference 42)	No (n = 69)	**5.8% (4)**	21.7% (15)	**1.5% (1)**
	Yes (n = 69)	**23.2% (16)**	34.8% (24)	**18.8% (13)**
	p*	**.007**	.13	**.001**

* p-value from chi-square analyses comparing physically inactive vs active and obese vs. not obese.

Table 3

Multivariate analysis: Odds of cognitive impairment conferred by physical inactivity and obesity

	Total	Memory	Executive function
Step 1: Inactivity and obesity in separate models, with covariates*			
Inactivity	2.0 (0.6, 6.3)†	1.9 (0.8, 4.5)	**9.0 (1.8, 45.6)**
Obese by DXA	**3.4 (1.0, 11.8)**	1.5 (0.7, 3.3)	**14.3 (1.5, 139.9)**
Step 2: Combined inactivity + obesity, with covariates			
Inactivity	1.8 (0.6, 5.9)	1.8 (0.7, 4.4)	**9.4 (1.7, 52.8)**
Obese by DXA	3.3 (0.9, 11.4)	1.4 (0.6, 3.3)	**14.8 (1.4, 151.0)**

*Covariates = education, race, disease activity as measured by the SLAQ (49, 50), oral glucocorticoid use, and depression.

†Odds ratio (95% confidence interval)

Table 4

Bivariate analysis: Associations of anthropometric measures of obesity with cognitive impairment

		% (n) impaired		
		Total	**Memory**	**Executive function**
BMI≥30 kg/m^2	No (n = 96, 70.1%)	10.4% (10)	24.0% (23)	7.3% (7)
	Yes (n = 41, 29.9%)	24.4% (10)	36.6 (15)	17.1% (7)
	p*	0.06	0.15	0.12
BMI≥26.8 kg/m^2 (19)	No (n = 79, 57.7%)	**8.9% (7)**	21.5% (17)	**3.8% (3)**
	Yes (n = 58, 42.3%)	**22.4% (13)**	36.2% (21)	**19.0% (11)**
	p*	**0.03**	0.08	**0.008**
Waist circumference ≥88 cm	No (n = 81, 59.1%)	**8.6% (7)**	23.5% (19)	**3.7% (3)**
	Yes (n = 56, 40.9%)	**23.2% (13)**	35.7% (20)	**19.6% (11)**
	p*	**0.03**	0.13	**0.004**
Waist circumference ≥84.5 cm (19)	No (n = 72, 52.5%)	**6.9% (5)**	23.6% (17)	**2.8% (2)**
	Yes (n = 65, 47.5%)	**23.1% (15)**	33.9% (22)	**18.5% (12)**
	p*	**0.01**	0.19	**0.004**

*p-value from chi-square analyses comparing physically inactive vs active and obese vs. not obese.

Table 5

Multivariate analysis*: Odds of cognitive impairment conferred by physical inactivity and anthropometric measures of obesity

	Total	Memory	Executive function
Step 1: Obesity measures in separate models, with covariates			
BMI≥30 kg/m^2	1.6 (0.5,5.0)†	1.2 (0.5, 2.9)	1.0 (0.2, 4.0)
BMI≥26.8 kg/m^2	1.5 (0.5, 4.8)	1.4 (0.6, 3.3)	3.3 (0.7, 15.0)
Waist circumference ≥ 88 cm	1.9 (0.6, 6.1)	1.2 (0.5, 2.8)	4.2 (0.9, 20.1)
Waist circumference ≥ 84.5 cm	2.7 (0.8, 8.9)	1.2 (0.5, 2.7)	**5.5 (1.0, 31.0)**
Step 2: Combined inactivity + obesity measures, with covariates			
Inactivity	1.9 (0.6, 6.1)	1.9 (0.8, 4.7)	**9.1 (1.8, 46.7)**
BMI≥30 kg/m^2	1.5 (0.5, 4.9)	1.1 (0.5, 2.8)	0.8 (0.2, 3.7)
Inactivity	1.9 (0.6, 6.0)	1.8 (0.7, 4.5)	**8.1 (1.6, 41.8)**
BMI≥26.8 kg/m^2	1.4 (0.5, 4.5)	1.3 (0.6, 3.2)	2.7 (0.6, 13.1)
Inactivity	1.8 (0.6, 6.0)	1.9 (0.8, 4.6)	**7.9 (1.5, 41.0)**
Waist circumference ≥ 88 cm	1.8 (0.6, 5.7)	1.1 (0.5, 2.6)	3.2 (0.7, 16.0)
Inactivity	1.8 (0.5, 5.8)	1.9 (0.8, 4.6)	**8.4 (1.6, 44.3)**
Waist circumference ≥ 84.5 cm	2.6 (0.8, 8.4)	1.1 (0.5, 2.6)	4.8 (0.8, 27.7)

*Covariates = education, race, disease activity as measured by the SLAQ (49, 50), oral glucocorticoid use, and depression.

†Odds ratio (95% confidence interval)