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Perceived Cognitive Function in Systemic Sclerosis

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ABSTRACT

Objectives. Perceived cognitive dysfunction is prevalent in patients with systemic sclerosis (SSc) but not well-understood. This study aimed to examine potential factors associated with perceived cognitive function and to investigate the contributions of perceived cognitive function and symptoms to functional measures.

Methods. A cross-sectional survey was conducted among patients with SSc (N = 106). Participants were mainly female (84%) and White (82%). Perceived cognitive function, symptoms, and functional measures were assessed with PROMIS measures. A multivariable regression was conducted to identify factors associated with perceived cognition. Hierarchical linear regressions examined the unique contributions of perceived cognitive function and symptoms to social participation and physical function.

Results. Fifty-nine (56%) patients with SSc perceived mild to severe cognitive dysfunction. Being on work disability and having more fatigue were both significantly associated with perceived cognitive dysfunction. When examining the contributions of cognition and other symptoms to functional measures, self-reported cognition became nonsignificant after fatigue and pain were entered into the regression model.

Conclusion. Being on work disability and having more fatigue were most highly associated with perceived cognitive dysfunction in patients with SSc. Unlike fatigue and pain, perceived cognitive function was not independently associated with functional measures. Nonetheless, future research should disentangle cognitive function and other symptoms as well as their effects on daily activities in SSc.

SIGNIFICANCE AND INNOVATIONS (2-4 bullet points)

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- This is the first study examining potential factors associated with perceived cognitive function and investigating the unique contributions of perceived cognitive function and symptoms to functional measures of social participation and physical function in patients with SSc.
- Being on work disability and having greater fatigue are factors most strongly associated with perceived cognitive dysfunction in patients with SSc.
- After accounting for age and SSc subtype, perceived cognitive function explains an additional 21% and 22% of the variance in social participation and physical function, respectively.

Systemic sclerosis (SSc) is a rare autoimmune disease characterized by inflammation, vascular abnormalities, and fibrosis of the skin and internal organs (1). Aside from cardinal symptoms, patients often report chronic fatigue (2), pain (3), sleep disturbance (4), and psychological distress (5,6). These symptoms interfere with the ability to perform everyday life activities (7–13). Although therapy and medical treatments can alleviate some clinical disease manifestations, patients with SSc face challenges in self-managing symptoms (14,15). No cure exists for SSc, but self-management programs can minimize the impact of the disease and optimize physical and psychological health (16–20). Despite these efforts, evidence suggests that cognitive impairment is a significant, though an understudied part of symptom experience in patients with SSc (21–23). Without a better understanding of cognitive dysfunction in SSc, health providers might not be able to address it as part of symptom management programs.

Perceived cognitive dysfunction is among the most bothersome symptoms in patients who have SSc (23). Up to 87% of individuals with SSc have cognitive impairment that often affect memory and executive function (24,25). Although research suggests an association between dementia and SSc (26), the factors underlying cognitive impairment in patients with SSc remain unclear. Individuals with SSc attribute some of their cognitive problems to common symptoms of the disease, including hand pain, fatigue, sleep problems, and psychological distress (27). Cognitive problems may impact abilities to perform essential daily activities. For example, SSc patients often described having difficulties with finding the right words while in conversations and having trouble learning new information at work (27). In other rheumatic diseases, perceived cognitive dysfunction has been associated with fatigue, pain, and depression (28–33). Patients with systemic lupus erythematosus (SLE) or rheumatoid arthritis (RA) experiencing cognitive dysfunction reported difficulties with social and physical functioning

(34,35). Specifically, cognitive dysfunction was associated with poor physical performance in handgrip strength and gait speed (36,37).

Clearly identifying potential factors and symptoms associated with perceived cognitive dysfunction in patients with SSc could enable adequate strategies to manage or reduce this problem. Due to high symptom burden in patients who have SSc, perceptions of cognitive dysfunction might be driven by co-occurring symptoms rather than being the direct result of the disease process. Thus, evaluating the respective contributions of perceived cognitive dysfunction and symptoms to functional measures will expand the current understanding of the relationship between bothersome symptoms and daily life functioning. This study aimed to 1) determine potential factors (i.e., demographics, SSc characteristics, symptoms) associated with perceived cognitive dysfunction and 2) investigate the contributions of perceived cognitive function and symptoms to functional measures of social participation and physical function in people with SSc.

PATIENTS AND METHODS

Study participants. Participants were recruited from a scleroderma clinic at an academic medical center through referrals from a rheumatologist (DK), an existing SSc research registry (N = ~400) (contacted via email), and flyers posted on scleroderma social media pages. Interested people were screened over the phone for eligibility. One hundred and six patients with SSc enrolled between September 2021 and January 2022. Patients were eligible if they were age ≥ 18 years, had physician-diagnosed SSc, could read and understand English, and accessed Internet-connected devices to complete online surveys. Exclusion criteria consisted of self-reported of any major comorbid neurological conditions that might influence cognitive function, self-declaration of current alcohol or recreational drug dependence, or prolonged (≥ 5 years) history of substance dependence (Figure 1). The Medical Institutional Review Board at the University of Michigan approved all study procedures (HUM00203946).

Measures. *Demographic and SSc characteristics.* Age, sex, race (White, African American, Asian), education level (high school graduates, some college, associate's degree, bachelor's degree, or master's degree or higher), employment status (full-time, part-time, homemaker, retired, or on disability), and SSc subtype (diffuse, limited, or overlap/other) and disease duration since the date of diagnosis (in both continuous years and categorical data: < 5 years; 5 – 10 years; or 11 or more years) were obtained by self-report.

Perceived cognitive function. Perceived cognitive function was assessed with the Patient-Reported Outcomes Measurement Information System (PROMIS) cognitive function ability 8a short form (38), which assesses everyday perceived cognitive function abilities in terms of concentration, sharpness, thinking speed, and memory functioning on a 5-point Likert scale (1=

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not at all to 5 = very much) in the past 7 days. The scale was scored as recommended and converted to a t-score, with a population mean of 50 and SD of 10, using PROMIS

HealthMeasures Scoring Service, available at

https://www.assessmentcenter.net/ac_scoringervice; a higher score indicates better perceived cognitive function. Compared to the general population (mean score, 50 ± 10), a score of 0.5 SD worse than the population mean is considered mild, while scores 1.0 to 2.0 SD worse than the mean are considered moderate to severe symptom severity (39).

Symptoms and daily life function. The PROMIS FACIT-Fatigue short form has 13 items that assess individuals' fatigue experience and its impact on their everyday lives on a 5-point Likert scale (40). The PROMIS pain interference short form has 4 items that assess pain interfere with daily activities, work around the home, social activities, and household chores on a 5-point Likert scale (41,42). The PROMIS sleep disturbance short form has 4 items that assess average sleep quality, sleep refreshing, problem with sleep, and difficulty falling sleep on a 5-point Likert scale (42,43). The PROMIS anxiety short form has 4 items that evaluate perceptions of fearfulness, excessive worries, having difficulty focusing on anything other than anxiety, and feeling that things are uneasy on a 5-point Likert scale (42,44). The PROMIS depression short form has 4 items that measure people's feelings of worthlessness, helplessness, depressed mood, and hopeless on a 5-point Likert scale (42,44). The PROMIS ability to participate in social roles and activities has 4 items that assess the ability to perform leisure activities with others, family, usual work (including work at home), and leisure activities with friends on a 5-point Likert scale (42). The PROMIS physical function short form has 4 items that assess difficulty with doing chores, going up and down stairs at a normal pace, going for a walk for at least 15 minutes, and running errands and shopping on a 5-point Likert scale (42). All scores were converted to t-

scores (population mean \pm SD 50 ± 10) via PROMIS HealthMeasures Scoring Service. A higher number indicates more of the domain being measured.

Statistical analysis. The assumptions of normality, linearity, and homoscedasticity were investigated by histograms and residual scatterplots. Continuous data with a normal distribution were described as means and SDs; categorical data were described as numbers and percentages. Descriptive statistics were used to characterize perceived cognitive function by demographics and SSc characteristics. An independent t-test was used to examine whether perceived cognitive function differed based on sex. One-way analyses of variance (ANOVA) were used to evaluate the differences in the mean of perceived cognitive function based on race, education levels, work status, SSc subtype, and SSc disease duration. Pearson's correlations to assess the associations between age and perceived cognitive function.

For the first study aim, a multivariable regression analysis was performed to identify which variables were associated with and explained the variation in perceived cognitive function. The analysis was controlled for demographics and SSc characteristics that previous literature associated with cognitive function. Specifically, we controlled for age (24), work status (27), SSc subtype (25), and disease duration (22,25).

For the second study aim, two hierarchical linear regression analyses were conducted to determine the contributions of perceived cognitive function and symptoms to functional measures of social participation and physical function. Age, work status, and SSc subtype, which were found significant with the functional measures based on previous research (7,45), were entered in the first block to control for their effects on the remaining variables of interest. As perceived cognitive functioning has not yet been investigated in SSc, the relationship was

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unknown and therefore entered in the second block. Psychological symptoms (i.e., anxiety, depression) were entered next, as significant findings were found in the literature (12,13), and the common SSc symptoms (23) (i.e., fatigue, pain, sleep disturbance) entered last as we expected a strong relationship between these symptoms and functional measures based upon previous studies (7,9). This method of entry allows us to assess what the addition of each new variable contributes to the explanation of functional measures at each step of the model. The statistical significance level was set at $P < 0.05$. All statistical analyses used SPSS version 27.0.

RESULTS

Participant characteristics. Table 1 shows characteristics of the 106 patients with SSc included in the analysis. More than half (58%) had the diffuse SSc subtype. The mean disease duration was 8 years, with 51% having early disease duration (34 diffuse and 19 limited), within 5 years of SSc diagnosis. The mean PROMIS score on perceived cognitive function was 45.8, with 59 (56%) participants with SSc scoring in the mild to severe cognitive impairment range. For the PROMIS symptom measures, the fatigue score was 0.8 SD (t-score = 57.7) worse than U.S. norm and pain score was 0.6 SD (t-score = 55.9) worse than U.S. norm. Other scores on sleep disturbance, anxiety, and depression fell within 0.5 SD of U.S. norm. Regarding functional measures, scores on social participation (t-score = 45.8) and physical function (t-score = 41.8) indicated that sample means were 0.5 SD and nearly 1.0 SD worse than U.S. norm.

Perceived cognitive function by demographics and SSc characteristics. Table 2 shows mean perceived cognitive function across demographics and SSc characteristics. Participants' perceived cognitive function was significantly differed based on their work status ($F(4,101) = 25.17, P = 0.008$). Perceived cognitive function did not differ in the sample when based on race, education levels, SSc subtypes, or SSc duration. Results from an independent t-test indicated that there was no significant effect for sex ($t(104) = 1.2, P = 0.229$), despite male participants ($M = 48.3, SD = 10.6$) reporting higher scores than female participants ($M = 45.3, SD = 9.0$). Pearson's correlations showed that age was not significantly associated with perceived cognitive function ($r = 0.18, P > 0.05$).

Factors associated with perceived cognitive function. Table 3 shows results from a multivariable regression analysis. Older age was significantly associated with perceived better

cognitive function ($B = 0.19$, 95% confidence interval [CI] 0.02 to 0.36, $P = 0.032$). Being on work disability was significantly associated with a lower level of perceived cognitive function ($B = -5.41$, 95% CI -10.07 to -0.75, $P = 0.023$). Participants who reported higher fatigue had significantly worse cognitive function ($B = -0.37$, 95% CI -0.66 to -0.08, $P = 0.014$), meaning a participant who scores 1 point higher on the PROMIS fatigue scale scored on average 0.4 points lower on the perceived cognitive function scale. Although the effect size is not relatively large, fatigue was the only symptom that was associated with perceived cognitive function. The model explained 42% of the variance in perceived cognitive function scores ($R^2 = 0.42$; $F(14, 91) = 4.76$; $P < 0.001$). We further examined the interaction between age, being on work disability, and fatigue. The interaction between these variables was not significant.

Contributors to social participation. Table 4 shows the results from the hierarchical regression models. Model 1 indicated that 2% of the variance in social participation was explained by age and SSc subtype ($R^2 = 0.02$, $F(3, 102) = 0.66$, $P > 0.05$). In model 2, the addition of perceived cognitive function led to an additional 21% of the explained variance in social participation ($R^2 = 0.23$, $F(4, 101) = 7.40$, $P < 0.001$). In model 3, anxiety and depression added 16% of the explained variance to social participation with $R^2 = 0.39$, $F(6, 99) = 10.58$, $P < 0.001$. In model 4, the addition of fatigue, pain interference, and sleep disturbance to the regression model, allowed an additional 21% of the explained variance in social participation ($R^2 = 0.60$, $F(9, 96) = 16.09$, $P < 0.001$). With the addition of fatigue and pain interference in model 4, perceived cognitive function became nonsignificant. Fatigue ($B = -0.44$, 95% CI -0.65 to -0.24, $P < 0.001$), pain interference ($B = -0.24$, 95% CI -0.43 to -0.05, $P = 0.014$), and anxiety ($B = -0.31$, 95% CI -0.53 to -0.10, $P = 0.004$) significantly predicted worse social participation, with

the strongest contributor being fatigue. In sum, the final regression model statistically significantly predicted social participation and explained 60% of the variance in social participation.

Contributors to physical function. Table 5 shows the results from the hierarchical regression models. Model 1 indicated that 3% of the variance in physical function was explained by age and SSc subtype ($R^2 = 0.03$, $F(3, 102) = 1.10$, $P > 0.05$). In model 2, the addition of perceived cognitive function led to an additional 22% of the explained variance in physical function ($R^2 = 0.25$, $F(4, 101) = 8.32$, $P < 0.001$). In model 3, anxiety and depression added 12% of the variance in model 3 to the explanation of physical function with $R^2 = 0.37$, $F(6, 99) = 9.62$, $P < 0.001$. In model 4, the addition of fatigue, pain interference, and sleep disturbance to the regression model allowed an additional 22% of the variance in physical function to be explained ($R^2 = 0.59$, $F(9, 96) = 15.53$, $P < 0.001$). With the addition of fatigue and pain interference in model 4, perceived cognitive function became nonsignificant. Fatigue and pain interference significantly predicted poor physical function ($B = -0.23$, 95% CI -0.44 to -0.02, $P = 0.032$ and $B = -0.44$, 95% CI -0.64 to -0.25, $P < 0.001$, respectively), the strongest contributor being pain interference. In conclusion, the final regression model statistically significantly predicted physical function and explained 59% of the variance in physical function.

A post hoc analysis was performed to examine how the order in which symptom variables were entered into the model influenced their contributions to variance in functional measures. In these models, perceived cognitive function was entered last to examine if any further variance in social participation or physical function was explained by perceived cognitive function above and beyond the effects of work status and other symptoms. The results revealed

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that no additional variance in social participation and physical function was explained by perceived cognitive function.

DISCUSSION

Perceived cognitive dysfunction in patients with SSc are prevalent (21,22,24,25), yet this domain is not well-understood. This study is among the first to examine how demographics, SSc characteristics, and symptoms experienced relate to perceived cognitive function in people with SSc. Over half (56%) of participants experienced mild to severe cognitive impairment in our study. Contrary to previous research (24), we found that older age was significantly associated with better perceived cognitive function. Since older participants were mostly retired, their daily life tasks might not require much cognitive capability compared to working-age participants. Thus, they might not notice changes in cognitive function. Besides being older, being on work disability was associated with perceived cognitive dysfunction. One explanation could be that being on work disability is associated with high symptom burden such as fatigue and pain (10). Such symptoms often cause low energy and poor concentration (27,28). Patients with SSc who had overlapping rheumatic conditions (referred to as overlap SSc) reported the worst perceived cognitive function, followed by diffuse and then limited cutaneous SSc, but the differences were not significant. This finding concurs with another study that did not find significant differences on cognitive impairment regarding SSc subtype (25). Despite the trend that perceived cognitive dysfunction might be reflective of disease symptom burden, the subsample of participants with overlap SSc was relatively small, and statistical power could explain the lack of statistical significance.

In examining the associations of common symptoms with perceived cognitive function, fatigue was uniquely associated with perceived cognitive dysfunction, though the effect size was not large. These findings support a previous qualitative study in which participants with SSc reported that their fatigue and cognitive difficulties are linked (27). Similar findings were found

in a qualitative study among patients with SLE (33). Although fatigue and pain are highly associated, the current study did not find a significant association between pain with perceived cognitive function. Pain might be related to specific cognitive domains rather than the general cognitive function as other studies found associations between pain and executive functioning in people with RA (28) and pain and functional memory (30). Additionally, the current study did not find a significant association of sleep disturbance with perceived cognitive function, similar to a previous study in patients with chronic pain (30). It is possible that cognitive function could be associated with specific sleep-related variables such as daytime sleepiness as in a previous study in patients with rheumatic diseases (46). Contrary to previous research on SSc (27) and fibromyalgia (29), anxiety and depression were not associated with perceived cognitive function in the current study. One explanation could be that our sample fell within the normal range of anxiety and depression (mean t-scores = 53.4 and 51.5, respectively). Moreover, previous studies used different measures, including the State-Trait Anxiety Inventory and the Beck Depression Inventory, to assess anxiety and depression, respectively. Different and diverse measures for assessing psychological symptoms could induce different results (47), though PROMIS measures have been recommended for use in to monitor patients' health in rheumatic diseases (48).

Our study is also the first to investigate the unique contributions of perceived cognitive function and symptoms to functional measures. Although perceived cognitive function has been significantly associated with social participation in SLE (34), this was only partly the case in our SSc sample. Initially, the addition of the perceived cognitive function in the statistical model added a significant contribution above and beyond age, SSc subtype, anxiety, and depression. However, the contribution became insignificant after adding fatigue and pain. These findings suggested that symptoms do not occur in isolation but are rather co-occurring (23). However,

while symptom experience in SSc appears to be multifaceted, further study is necessary in order to provide a better understanding of how symptoms interrelate and affect the ability to participate in social roles and activities.

Similar to social participation, the initially significant association between perceived cognitive function and physical function dissipated when fatigue and pain were added to the regression model. The heterogeneity of deficits in cognition might explain why perceived cognitive function was no longer associated with physical function. That is, a specific cognitive domain might be associated with physical function. For instance, patients with SSc complained that short-term memory problems limited their ability to run errands or shop (items included in physical function measures), whereas concentration and focus could associate more closely with other daily life activities such as driving and reading in people with SSc (27). Thus, it becomes important to emphasize the need to assess cognitive performance across different domains in people with SSc and examine effects of different domains to physical function.

Similar to previous SSc studies (7,8), the current study found that fatigue and pain severity was associated with decreased social participation and physical function. Although intervention programs currently help to manage and reduce fatigue (17,18), fatigue's impact on cognitive function and reduced daily life activities remains problematic in people with SSc. Participants with higher levels of pain reported lower levels of social participation and physical function, consistent with previous SSc research (7,23). Pain can influence social participation levels, possibly because of disturbing consequences associated with pain experience. For instance, patients who have SSc might avoid attending outdoor events with friends and family due to cold weather, which could trigger Raynaud's Phenomenon and cause pain (23,49). Pain might cause concentration problems and difficulties with learning new information at work (27),

as the ability to perform work is part of social participation measure. Additionally, constant pain causes cognitive deficits in thinking (27), thus patients with SSc might avoid common errands such as grocery shopping and yard work that require organization of thoughts. These results suggest that perceived cognitive difficulties might be an underlying factor in the association between pain and functional measures.

This study had several limitations. First, convenience sampling was used, potentially limiting the representativeness of the final SSc sample obtained. Participants were predominantly from the SSc registry and SSc social media, particularly from one community support group where an academic medical scleroderma clinic is based, suggesting possible selection bias. It is likely that participants who readily respond to an online computer survey are more motivated, more highly educated, have fewer hand limitations (e.g., ability to type), and may have higher cognitive capacity to complete the questionnaires. Nevertheless, even among this sample, our results show that the magnitude of cognitive dysfunction was significant. Second, it was impossible to ascertain the temporal association between being on disability and cognitive dysfunction in the current cross-sectional study, though previous research in SSc reported that perceived cognitive dysfunction was associated with unemployment (27). Additionally, it was not possible to determine the causality between perceived cognitive function, symptoms, and daily life functioning. Third, self-reported measurements, particularly for evaluating cognitive function, have their own inherent concerns such as recall bias. However, collecting patient-reported data is an effective way to better understand symptom experience and identify often-overlooked problems. Fourth, a large majority of respondents to this survey were female and White, again potentially reducing the generalizability of the study. Importantly, small sample sizes in several sub-categories, such as male sex and race/ethnicity minorities, caused a lack of

statistical power to detect statically significance. Still, this study added to a paucity of research in perceived cognitive function in patients with SSc. Along with perceived cognitive function, fatigue and pain are particularly important in understanding daily life functioning in people with SSc. As such, studies are needed to disentangle cognition and common SSc symptoms and their effects on daily life functioning through a combination of subjective and objective measures (e.g., cognitive function) and repeated assessments across consecutive days. It is likewise important to investigate which cognitive domains are significantly associated with functional measures. For a more comprehensive investigation of cognition, future research must assess impacts from SS-related treatments (e.g., immunosuppressive therapy) and other important SSc-related symptoms (e.g., cardiac involvement, interstitial lung disease, gastrointestinal symptoms, dyspnea, skin thickening severity) on cognitive function. With this, researchers and health professionals can develop intervention programs for targeted patients. Additionally, studies should also examine the impact of cognitive difficulties beyond functional measures to quality of life, work limitation, and driving to compare whether the findings agree with previous qualitative research regarding perceived cognitive difficulties in patients with SSc (27). Finally, some alternative approaches to gathering data and more representative sampling (e.g., male sex, race/ethnicity minority, those without computer or Internet access, or those not connected with SSc centers) should be considered in future research.

In conclusion, although perceived cognitive function associated with both functional measures when controlling for demographics and psychological symptoms, perceived cognitive function became insignificant when fatigue and pain were included in our multivariable model. A more comprehensive study is needed to better understand symptom experience in SSc by

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disentangling cognition from other symptoms in time and examining their influence on everyday functioning.

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Figure 1. Participant flow diagram.

Table 1 Descriptive data for all variables (N = 106)

		Min – Max
Age, mean (SD), years	55.2 (11.5)	25.0 – 76.0
Female, n (%)	89 (84)	
Race, n (%)		
White	87 (82)	
African American	14 (13)	
Asian	5 (5)	
Education levels, n (%)		
High school degree	9 (8)	
Some college	22 (21)	
Associate's degree	18 (17)	
Bachelor's degree	36 (34)	
Master's or higher	21 (20)	
Work status, n (%)		
Full-time employed	33 (31)	
Part-time employed	6 (6)	
Homemaker	12 (11)	
Retired	28 (26)	
On disability	27 (26)	
SSc subtype, n (%)		
Diffuse	62 (58)	
Limited	39 (37)	
Overlap and other (1 SINE)	5 (5)	
Disease duration, mean (SD), years	8.1 (7.4)	0.5 – 35
0 – 5 years, n (%)	54 (51)	
6 – 10 years, n (%)	24 (23)	
11+ years, n (%)	28 (26)	
Perceived cognitive function, mean (SD)	45.8 (9.3)	27.9 – 66.7
Symptom (PROMIS score), mean (SD)		
Fatigue	57.7 (9.0)	30.3 – 75.1
Pain interference	55.9 (8.7)	41.6 – 75.6
Sleep disturbance	54.1 (8.3)	32.0 – 73.3
Anxiety	53.4 (8.3)	40.3 – 73.8
Depressed mood	51.5 (9.0)	41.0 – 75.6
Functional measure (PROMIS score), mean (SD)		
Social participation	45.9 (8.1)	27.5 – 64.2
Physical function	41.8 (8.3)	29.1 – 56.9

Note. SSc = systemic sclerosis. PROMIS = Patient-Reported Outcomes Measurement Information System. To all PROMIS scores, a higher score indicates more of the trait being measured. Compared to the general population (mean score, 50 ± 10), a score of 0.5 SD worse than the population mean is considered mild, and scores 1.0 to 2.0 SD worse than the mean are considered moderate to severe symptom severity.

Table 2 Demographic and SSc characteristics of the participants and their association with perceived cognitive function (N = 106)

	Perceived cognitive function mean (SD)	P-value
Sex		0.229
Female	45.3 (9.0)	
Male	48.3 (10.6)	
Race		0.699
White	46.1 (9.2)	
African American	45.3 (11.4)	
Asian	42.5 (1.9)	
Education levels		0.526
High school degree	48.2 (13.4)	
Some college	44.3 (6.0)	
Associate's degree	43.4 (9.6)	
Bachelor's degree	46.2 (9.6)	
Master's or higher	47.6 (9.6)	
Work status		0.008
Full-time employed	47.8 (9.3)	
Part-time employed	46.3 (12.9)	
Homemaker	48.3 (10.3)	
Retired	47.6 (7.9)	
On disability	40.2 (7.5)	
SSc subtype		0.729
Diffuse	45.6 (9.4)	
Limited	46.4 (9.4)	
Overlap	43.1 (8.1)	
Disease duration		0.503
0 – 5 years	45.0 (9.5)	
6 – 10 years	45.5 (9.6)	
11+ years	47.5 (8.8)	

Note. Perceived cognitive function was measured via PROMIS short forms. The p-value for sex variable was calculated based on t-test. All other p-values were calculated based on ANOVA tests.

Perceived Cognitive Function in Systemic Sclerosis

Table 3 Summary of multivariable regression analysis to determine factors associated with perceived cognitive function (N = 106)

Independent variable	Unstandardized B (95% CI)	Standardized β	t	P-value
Age	0.19 (0.02, 0.36)	0.23	2.17	0.032
Work status ^a				
Part-time employed	-1.55 (-8.48, 5.39)	-0.04	-0.44	0.659
Homemaker	-0.26 (-5.68, 5.16)	-0.01	-0.10	0.923
Retired	-4.81 (-9.86, 0.25)	-0.23	-1.89	0.062
On disability	-5.41 (-10.07, -0.75)	-0.25	-2.31	0.023
SSc subtype ^b				
Diffuse	-2.06 (-9.53, 5.41)	-0.11	-0.55	0.585
Limited	-1.57 (-9.37, 6.23)	-0.08	-0.40	0.690
Disease duration ^c				
0 – 5 years	-3.68 (-7.50, 0.14)	-0.20	-1.91	0.059
6 – 10 years	-4.10 (-8.53, 0.33)	-0.19	-1.84	0.069
PROMIS score				
Fatigue	-0.37 (-0.66, -0.08)	-0.36	-2.50	0.014
Pain interference	-0.26 (-0.54, 0.01)	-0.25	-1.91	0.059
Sleep disturbance	0.14 (-0.07, 0.35)	0.13	1.36	0.176
Anxiety	0.05 (-0.25, 0.36)	0.05	0.35	0.725
Depressed mood	-0.03 (-0.35, 0.29)	-0.03	-0.18	0.858

$R^2 = 0.42$. 95% CI = 95% confidence interval.

a.Reference group was full-time employed. b.Reference group was overlap SSc subtype.

c.Reference group was having SSc more than 11 years.

Perceived Cognitive Function in Systemic Sclerosis

Table 4 Summary of final hierarchical regression analyses for variables associated with social participation (N = 106)

Independent variable	Unstandardized B (95% CI)	Standardized β	R ²	R ² Change
Model 1			0.02	0.02
Age	-0.04 (-0.13, 0.06)	-0.05		
SSc subtype ^a				
Diffuse	-0.56 (-5.67, 4.57)	-0.03		
Limited	-0.63 (-5.85, 4.59)	-0.04		
Model 2			0.23	0.21
Perceived cognitive function	0.05 (-0.09, 0.19)	0.06		
Model 3			0.39	0.16
Psychological symptoms				
Anxiety	-0.31 (-0.53, -0.10)	-0.32**		
Depression	0.16 (-0.06, 0.38)	0.17		
Model 4			0.60	0.21
General symptoms				
Fatigue	-0.44 (-0.65, -0.24)	-0.49**		
Pain interference	-0.24 (-0.43, -0.05)	-0.25*		
Sleep disturbance	0.06 (-0.09, 0.21)	0.06		

95% CI = 95% confidence interval.

^aReference group was overlap SSc subtype. *P < 0.05; **P < 0.01.

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Table 5 Summary of final hierarchical regression analyses for variables associated with physical function (N = 106)

Independent variable	Unstandardized B (95% CI)	Standardized β	R ²	R ² Change
Model 1			0.03	0.03
Age	-0.04 (-0.14, 0.06)	-0.06		
SSc subtype ^a				
Diffuse	4.32 (-0.97, 9.61)	0.26		
Limited	5.13 (-0.26, 10.53)	0.30		
Model 2			0.25	0.22
Perceived cognitive function	0.06 (-0.08, 0.21)	0.07		
Model 3			0.37	0.12
Psychological symptoms				
Anxiety	0.05 (-0.16, 0.27)	0.06		
Depression	-0.10 (-0.33, 0.13)	-0.11		
Model 4			0.59	0.22
General symptoms				
Fatigue	-0.23 (-0.44, -0.02)	-0.25*		
Pain interference	-0.44 (-0.64, -0.25)	-0.47**		
Sleep disturbance	-0.002 (-0.15, 0.15)	-0.002		

95% CI = 95% confidence interval.

^aReference group was overlap SSc subtype. *P < 0.05; **P < 0.01.