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ACADEMIC OUTCOMES IN CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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Abstract

Objective—To explore academic outcomes in childhood-onset systemic lupus erythematosus (cSLE) and their relationship to variables such as demographic and socioeconomic status, neurocognitive functioning, behavioral/emotional adjustment, and cSLE disease status.

Methods—Forty pairs of children diagnosed with cSLE and healthy best-friend controls were rated by parents on a standardized scale of school competence. Information about participants' demographic and socioeconomic status was obtained, along with measures of cSLE disease activity and damage. All participants received formal neurocognitive testing and were also rated on standardized scales of behavioral/emotional adjustment and executive functioning.

Results—Compared to healthy controls, school competence was rated as lower in the cSLE group, although the groups did not differ significantly on indices of cognitive, behavioral, emotional, or executive functioning. School competence ratings were correlated with reading and mathematics achievement test scores in both groups, and with ratings of mental self-regulation in the cSLE group. School competence ratings were correlated with measures of cSLE disease activity and treatment intensity.

Conclusion—cSLE is associated with inferior parent-rated academic outcomes compared to those noted in demographically-matched peers, despite similar neurocognitive function. The adverse academic outcomes which distinguish children with cSLE from their demographically-matched peers appear to be mediated by SLE disease activity and treatment.

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AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Ying had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Keywords

SLE; Children; cognition; NPSLE

INTRODUCTION

Systemic lupus erythematosus (SLE) is associated with significant morbidity, negatively affecting health-related quality of life (HRQoL) (1). Academic functioning represents a critical aspect of HRQoL in childhood and adolescence. However, it has attracted surprisingly limited research interest, despite concerns that children with SLE who perform poorly in school go on to meet fewer educational milestones (e.g., high school or college graduation), have less long-term occupational success, and experience higher rates of adult mental illness and substance abuse (2-6). The available data suggest that children with cSLE (childhood-onset systemic lupus erythematosus) are at risk for adverse academic outcomes (1,7,8). If cSLE affects academic functioning, then it is important to explore the mechanisms that underlie this effect and incorporate this knowledge into disease management.

In adults, adverse effects of SLE have been shown to impair cognitive and psychiatric functioning (9). Despite reports that cSLE is associated with cognitive deficits (10) and psychiatric morbidity (11,12), most previous studies have been limited to chart reviews lacking a well-matched control group. Conversely, a recent case-control study found the rate of neurocognitive dysfunction (NCD) in cSLE to be elevated relative to general population norms but comparable to that of controls who were closely matched on demographic variables (13). This methodologically-rigorous study raises questions regarding the contribution of cSLE disease and treatment factors to cognitive and psychiatric morbidity. It also highlights the importance of exploring other factors besides NCD that might contribute to lower school functioning in patients with cSLE.

The current study used a case-control design to achieve three goals: (1) determine whether individuals with cSLE have worse academic functioning than their peers of similar demographic and socioeconomic backgrounds; (2) investigate whether these matched groups differ with respect to cognitive, behavioral, and emotional functioning; and (3) explore demographic, cognitive, behavioral, emotional, and disease-related correlates of school functioning within samples of children with cSLE and unaffected peers.

MATERIALS & METHODS

Subjects

Forty children and adolescents with cSLE and 40 same sex best-friend controls of similar demographic characteristics participated in a study of functional and structural neuroimaging and cognitive functioning in cSLE, conducted at two tertiary pediatric rheumatology centers. Analyses of neuroimaging data from the study will be presented in a separate report, and are not discussed herein.

All participants spoke English as their primary language. This study was approved by the institutional review boards of both institutions and is in accordance with the ethical standards established in the 1964 Declaration of Helsinki. Prior to participation, the study was explained to each participant and their parent, and written informed consent obtained from parents of all participants. Written assent was also obtained from all participants over 11 years of age.

Childhood-onset SLE—Participants with cSLE fulfilled the updated American College of Rheumatology classification criteria prior to 17 years of age (14). To be eligible for participation, a patient had to be between the ages of 9 and 18 at the time of enrollment in the study. Patients with cSLE were excluded from participation if they had a history of comorbid conditions affecting their neurocognitive functioning prior to the diagnosis of cSLE, and if they had known structural brain abnormalities, neuropathies, or movement disorders.

Controls—Each index patient with cSLE was asked to identify a friend who was within one year of their age, of the same gender, and in the same school grade. This “best-friend approach” has been shown to result in good case-control matches on demographic variables (15). Controls had to be healthy, without known structural brain abnormalities or known NCD. No potential controls needed to be excluded from participation by these criteria.

Study assessment

In this cross-sectional study, participants were evaluated during a dedicated research visit lasting approximately 3 to 4 hours. Besides a physical examination and a review of systems, all study participants underwent thorough neurocognitive assessment. Data collected during this research visit are described below.

Demographics—Demographic information related to ethnicity, maternal education, number of parents in household, and family income was collected by parent report.

Disease Activity and Severity (cSLE subjects only)—Disease activity was measured using the *SLEDAI-2K* (Systemic Lupus Erythematosus Disease Activity Index) and the *BILAG* (British Isles Lupus Activity Group Index), while disease damage was assessed using the *SDI* (Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index) (16,17). The daily dose of oral prednisone (if prescribed) was recorded as a surrogate of treatment intensity.

Academic Functioning—Academic functioning was assessed via the *School Competence scale* of the Child Behavior Checklist (CBCL), a standardized questionnaire completed by parents of study participants (18). Academic functioning can be difficult to measure due to lack of consistent access to original school records, variations in grading schemes across schools and grade/age levels, and the fact that academic knowledge (assessed via formal testing) is only one of several contributors to classroom performance. Consistent with our goal of assessing classroom performance relative to norms on a common metric, the CBCL School Competence scale is comprised of standardized ratings of the child's functioning across multiple academic domains (e.g., reading/language arts, arithmetic), as well as implementation of academic interventions. Ratings on the CBCL School Competence scale are converted to a single T-score based on age- and sex-linked norms, with higher scores indicating better functioning.

Table 1 provides descriptions of the other psychometric information obtained from participants via parent questionnaires and formal neurocognitive testing, along with the functional domains they measure. Further details about these measures are presented below.

Behavioral and Emotional Functioning—Participants’ behavioral and emotional functioning was obtained by parent report on the CBCL (18). Three CBCL indices were studied. The *Externalizing Problems index* assesses delinquent and aggressive behaviors. The *Anxious/Depressed subscale* focuses on mood symptoms and was chosen over the broader Internalizing Index because the latter includes physical symptoms that could reflect

legitimate medical concerns, rather than mood (19). The *Total Problems index* is an overall composite of behavioral and emotional concerns.

The Children's Depression Inventory was completed by participants as a self-report measure of depressive symptomatology (20).

Executive Functioning in Daily Life—Because executive functioning (e.g., behavior regulation, metacognitive skills such as planning and organization) can be very difficult to validly assess using formal one-on-one neuropsychological tests, parents completed the Behavior Rating Inventory of Executive Functioning (BRIEF) (21), a standardized questionnaire. The *Behavioral Regulation, Metacognition*, and *Global Executive Composite* scales of the BRIEF were considered in this study.

Formal Neurocognitive Testing—All participants underwent formal neurocognitive testing performed by a trained psychometrician, using a standardized neuropsychological battery for cSLE with details provided elsewhere (22). In brief, the battery consisted of the Wechsler Abbreviated Scale of Intelligence (WASI) (23) which is a well-validated measure of overall intelligence (*Full Scale IQ*); Working Memory and Processing Speed subscales of the age-appropriate Wechsler Intelligence Scales (24,25) which measure working memory and psychomotor speed, respectively; Wide Range Assessment of Memory and Learning-2 (WRAML-2) (26), from which the *Memory Screening Index* summarizes an individual's ability to learn and recall new verbal and visual information; selected subtests from the Woodcock-Johnson–III Tests of Achievement (27) which assessed basic reading/decoding ability (*WJ-III Letter-Word Identification)* and written arithmetic skills (*WJ-III Calculation);* and the Conners' Continuous Performance Test–II (28) which assesses test-takers' ability to sustain attention (CPT-II Omissions, CPT-II Mean Hit Reaction Time Standard Error) and inhibit impulsive responses (*CPT-II Commissions*) during a long, boring task. Age-normed scores are available for all instruments (22).

Statistical analysis—Primary analyses used paired-sample t-tests to compare means between the cSLE patients and their demographically matched best-friends (controls); and Pearson's correlation coefficients (r's) to assess relationships between continuous variables. In addition, nonparametric Wilcoxon's signed rank tests and Spearman's correlation coefficients were used as supplementary analyses for paired-sample t- tests and Pearson's r's, respectively. Multivariate analyses, including mixed effect models and partial correlation coefficients, were used to compare means and assess relationships after adjusting for social-demographic characteristics. Only results from primary analyses are presented in the paper, as there were no important discrepancies between nonparametric and parametric analyses. For categorical variables, associations with cSLE/control group membership were assessed using logistical models after adjusting for within-pair correlations using a GEE method. For numerical variables in the cSLE group, their means were compared to those of population norms using z-tests. Strength of correlation was considered "very strong", "strong", "moderate", "weak", and "poor" if the magnitude of r was 0.9~1, 0.7~0.9, 0.5~0.7, 0.3~0.5 and 0~0.3 respectively (29). Statistical computations were performed using a SAS 9.3 software (SAS, Cary, NC) package. P-values <0.05 were considered statistically significant.

RESULTS

Demographics of the study participants and disease information about the cSLE group are provided in **Table 2**. Patients with cSLE were somewhat older than the best-friend controls but otherwise the groups were closely matched on major demographic indices. The mean disease duration of the cSLE group was about 2 years, with mild to moderate disease

activity and disease-related damage. Prednisone therapy was used in 31 (77.5%) of the cSLE patients.

Academic functioning of cSLE and control groups

Parent-rated school competence, as measured by the CBCL, was significantly lower in the cSLE group than the control group (mean ± SD: 48.4 ± 9.2 versus 51.4 ± 5.1, p = 0.02). **Figure 1** presents a plot of the CBCL School Competence T-Score ratings for each cSLE best-friend control pair. Although the mean score for both groups fell within the normal range, greater variability is apparent in the cSLE group.

Comparisons between cSLE and control subjects on indices of cognitive, behavioral, emotional, and executive function

As shown in **Table 3**, the cSLE and demographically-matched control groups were not significantly different in their performance during formal neurocognitive testing or on measures of behavioral, emotional, or executive functioning (CBCL, BRIEF, CDI). Conversely, compared to published norms, the cSLE group had significantly *weaker* scores on the Wechsler Working Memory and Processing Speed Indexes, and significantly *better* scores than published norms on the CBCL Externalizing Problems and BRIEF Behavior Regulation indexes, and on the CDI Total Score of overall depressive symptoms.

Correlates of academic functioning

Table 4 summarizes the associations between CBCL School Competence ratings and the behavioral, emotional, executive and cognitive functioning of participants in the cSLE and matched control groups. Importantly, correlations of these variables with school competence did not differ significantly between the two groups. Variables that were associated with school performance in the cSLE group were, for the most part, similarly strongly associated in the control group. Not surprisingly, CBCL School Competence ratings were moderately correlated with performance on Woodcock-Johnson Achievement subtests measuring reading decoding and math calculation skills. Interestingly, while we observed expected weak correlations for the overall sample between School Competence ratings and the Wechsler Working Memory and Processing Speed indices, School Competence was not significantly correlated with measures of overall intelligence, sustained attention, or impulse control. Significant correlations were found, however, between School Competence ratings and the BRIEF Metacognition index and Global Executive Composite, within the cSLE group and in the overall sample.

In addition to the measures collected for all participants, we assessed the relationship between CBCL School Competence and measures of cSLE activity, damage and treatment intensity. As shown in **Table 5**, School Competence was significantly related to disease activity as indicated by both the SLEDAI and BILAG indices, and also to higher prednisone doses.

DISCUSSION

We found that children with SLE have significantly inferior academic outcomes than their peers, despite indistinguishable performance levels on neuropsychological tests and equivalent ratings of externalizing behavior, mood, and executive functioning. These academic outcome findings are in line with our previous research (1), which revealed parent-and self-report ratings of school functioning on the PedsQL™ to be significantly lower in cSLE than a normal national comparison sample (30). Our current results extend those findings to demonstrate an effect even when comparing patients with cSLE to demographically similar peers.

Given the importance of scholastic performance for children and adolescents, it is important to understand the mechanism by which cSLE might impair school functioning. Our findings indicate that disease activity and treatment intensity are significant correlates of poor school competence in patients with cSLE. Furthermore, cognitive variables that were associated with school competence in healthy controls had similar associations in children with cSLE: reading skill, mathematics skill, short-term attention/working memory, and mental processing speed. Importantly, although participants with cSLE scored differently than published norms on several outcome measures, this appears to be due to their demographic differences from the normative sample. The cSLE group did not significantly differ from demographically-matched controls on any cognitive, behavioral, emotional, or executive functioning measure. Thus, while poor school performance in any individual may relate to neuropsychological disturbance, we did not find evidence that such disturbances are the systematic mechanism by which cSLE results in diminished school performance. Based on the associations observed in our cross-sectional analyses, we can entertain two possible explanations for the difference in the academic functioning between children and adolescents with cSLE and their peers.

The most obvious explanation to consider is related to the adverse effect that cSLE-related symptoms and signs may have upon school participation. In our study, we clearly demonstrated that cSLE disease activity and prednisone treatment dose are related to worse academic outcomes. Although school attendance was not specifically measured in our study, it would make sense that cSLE patients with more active disease requiring more intense medication regimens are more likely to be absent from school than their less severely-affected counterparts. Earlier reports and our own registry data indicate an increased number of missed days of school in cSLE (31). This raises the possibility of a disruptive effect of cSLE as a chronic illness with acute episodes that interfere with children's functioning at school and in other performance contexts.

Second, although we did not identify significant differences between cSLE and the best-friend controls on formal neurocognitive measures, one cannot entirely exclude the possibility that cSLE disease activity or its treatment exerts a modest disruptive effect upon cognitive functioning, impacting school performance as a result. While the current sample of 40 children with SLE and 40 matched case-controls is the largest sample to date, our study might have been underpowered to detect subtle neurocognitive effects of cSLE on the performance of standardized tests such as the Wechsler Processing Speed Index.

The patients included in this study were mostly female, with mild/moderate disease activity approximately two years after diagnosis (32), and they reflected the diversity of SES commonly seen in cSLE (13,33). The high incidence of cSLE among U.S. ethnic and racial minorities makes a direct comparison to normative U.S. populations unfitting. Hence, we used a matched-control design to carefully select an appropriate comparison group that would enable us to better separate the impact of cSLE as a disease from that of socio-demographic effects. We are convinced that we achieved this, based upon the extremely similar demographic composition of the two groups. There was a statistically significant difference in age across the two groups, but because all of our major outcome measures were age-normed, the small age difference would not be expected to impact our results. This assumption is supported by our exploratory analyses which adjusted for age and found no substantive change in the findings reported.

Even though the current parent ratings and test results are within the average range, on a few measures both groups showed a trend to deviate from reference norms. For example, a deviation of 0.64 SD was noted in the cSLE group on the Wechsler Working Memory Index. While such differences may seem relatively small on an individual basis, their impact within

a population such as cSLE can be substantial. A shift of -0.64 SD of the distribution of scores in the cSLE group corresponds to a 248% increase in cSLE Working Memory performances falling in the deficient range. Thus, even seemingly modest differences in mean scores can result in dramatically increased numbers of children who exceed psychometric thresholds for clinical deviance. Given that cSLE disproportionately affects children of minority and lower socioeconomic status, this impact may be especially apparent.

Our failure to identify disproportionate levels of NCD in cSLE subjects relative to case-controls is consistent with the recent report of Williams et al 2011 (13) where the frequency of NCD was similar in cSLE compared to demographically-matched peers. The replication of this finding highlights the role of demographic and socioeconomic factors in cSLE, and the importance of considering how these confounding factors affect patients' HRQoL. In particular, these findings stress a key weakness of other studies that rely exclusively upon comparisons against published norms. If the sample being studied is demographically dissimilar to the normative group, findings may be misleading.

Limitations of the present study are acknowledged. First, our definition of academic outcome was based on a single measure (School Competence ratings) from a single informant source (parents). Ideally, a study of academic competence would benefit from the inclusion of additional indicators of academic outcome. Unfortunately, a definition of academic competence that is comprehensive, multi-informant based, objective, and consistent across educational settings is not currently available. While future investigators may consider more objective measures of academic functioning (e.g., copies of report cards), we caution that such an approach is not a panacea, as differences in grading standards across teachers, schools, and curricula would remain. Similarly, academic skills assessed in an artificial, office-based setting (i.e., individual achievement testing) at best approximate actual classroom performance, and tests of basic reading and math skills would not necessarily be sensitive to the impact of a disease with onset in middle to late childhood, when the focus of learning turns towards higher-level skills. Second, although this study assessed a broad range of cognitive, behavioral, and emotional functioning, we cannot rule out the possibility of constructs or measures that might be more sensitive to cSLE. Third, though the current sample represents the largest group yet of children and adolescents with SLE to be prospectively studied, the statistical power of our analyses was nevertheless limited by its size. Future multicenter investigations may address this shortcoming. Our experience with "best friend" case-control methodology, however, taught us that this approach can be extremely challenging to implement. Another limitation of the present study, that is more easily addressed, was our failure to obtain systematic information about school disruption. Future studies of academic outcome in cSLE should quantify the disruptive effect of cSLE upon school participation, using records of school attendance/absence and medical history of patients' hospitalizations and day treatment visits.

The current investigation carries several implications for clinical care in cSLE. First, because our data suggest that disease-related factors may significantly impede patients' academic progress, they highlight the importance of minimizing such disruption by optimizing patient care (e.g., minimizing missed school) and maximizing treatment adherence. Second, although we did not demonstrate systematic deficits of neurocognitive functioning in cSLE relative to demographically-matched peers, this does not mean that such deficits are absent in individual patients. Monitoring for such deficits continues to be an important component of routine patient care, even if the deficits are not clearly related to the disease process. Finally, the current study underscores the importance of considering socioeconomic/demographic variables in both research and clinical care of cSLE and other chronic diseases that are disproportionately seen in minority populations.

In summary, our results indicate that children and adolescents with SLE do in fact experience poorer academic outcomes than demographically-matched healthy peers, and that cSLE disease severity and treatment intensity are associated with school competence. However, neither neurocognitive functioning nor ratings of behavioral, emotional, and executive functioning appear to be the mechanism by which cSLE impacts school competence.

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SIGNIFICANCE & INNOVATION

Innovation

- This study found significantly inferior academic outcomes in children and adolescents with systemic lupus erythematosus (cSLE) than in demographically-matched controls.
- Elevated cSLE disease activity is significantly associated with inferior academic outcomes, though we did not find clear evidence that neurocognitive deficits mediate this relationship. Disruption of school attendance due to cSLE and its treatment may significantly impede patients' academic functioning.

Significance

- Management of cSLE should consider the disruptive effect of illness and treatment upon school attendance and performance, emphasizing the importance of minimizing such disruption by optimizing patient care and treatment adherence.

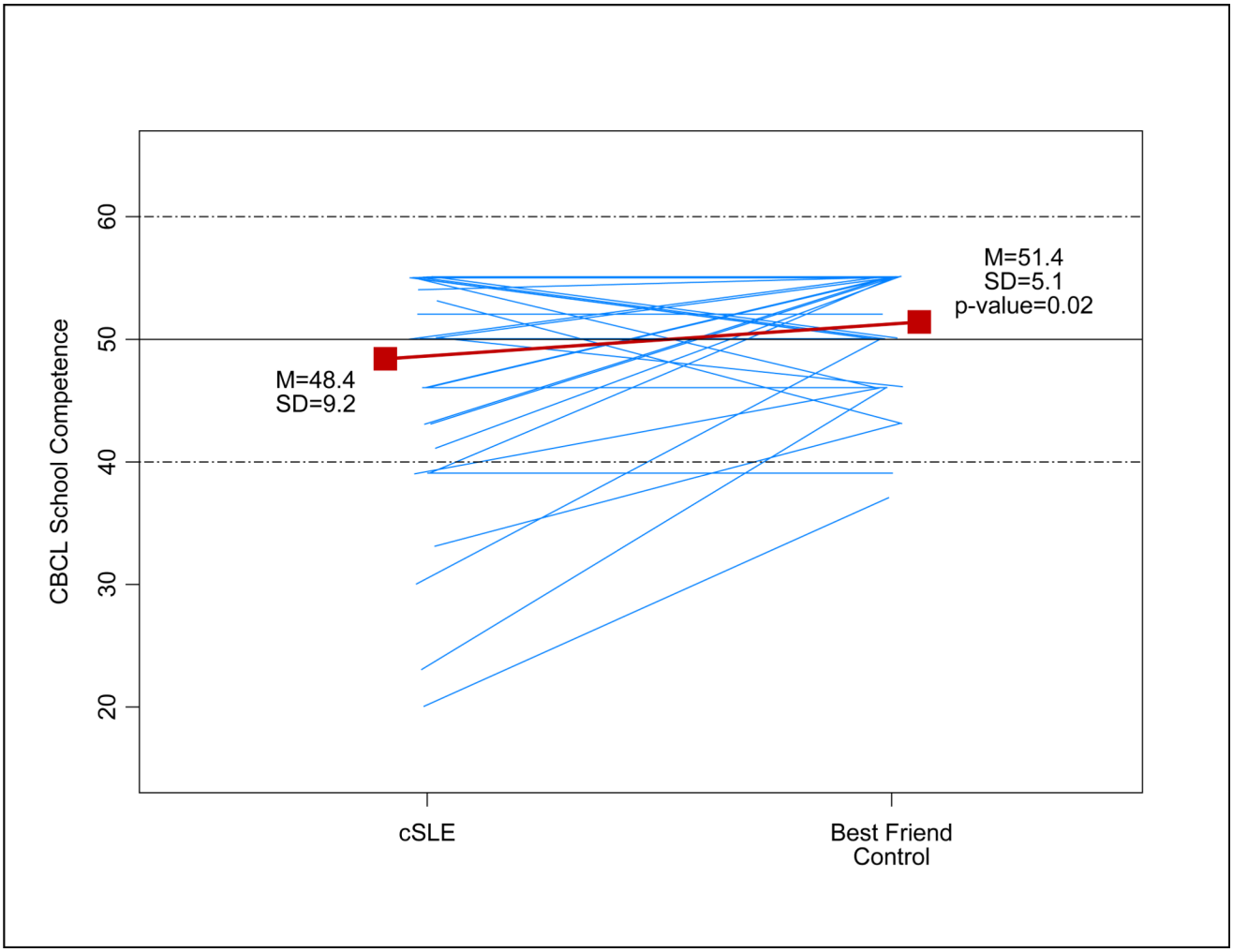

Figure 1. Plots of CBCL School Competence t -scores between cSLE's and paired best friends (controls)

Each blue line represents a cSLE-best friend pair; a red solid square represents the sample mean; the horizontal solid line represents the normative mean; and two doted lines represent ±1 normative standard deviation (SD) from the normative mean.

Table 1

Descriptions of psychometric variables

Name of Variable	Functional Domain	Population Norms (mean ± SD)	Valence (Higher Scores Reflect...)
Wechsler Abbreviated Scale of Intelligence (WASI): Full Scale IQ	General intelligence	100 ± 15	Better Functioning
Wechsler Intelligence Scales*: Working Memory Index	Working memory	100 ± 15	Better Functioning
Wechsler Intelligence Scales*: Processing Speed Index	Psychomotor speed	100 ± 15	Better Functioning
Wide Range Assessment of Memory and Learning-II (WRAML-II): Memory Screening Index	Verbal and visual memory	100 ± 15	Better Functioning
Woodcock-Johnson –III Tests of Achievement: Letter-Word Identification subtest	Reading decoding skills	100 ± 15	Better Functioning
Woodcock-Johnson –III Tests of Achievement: Calculation subtest	Arithmetic calculation skills	100 ± 15	Better Functioning
Conners Continuous Performance Test – II (CPT-II): Omissions	Attention	50 ± 10	Worse Functioning
Conners Continuous Performance Test – II (CPT-II): Commissions	Attention/impulsivity	50 ± 10	Worse Functioning
Conners Continuous Performance Test – II (CPT-II): Hit Reaction Time Standard Error	Attention	50 ± 10	Worse Functioning
Child Behavior Checklist (CBCL): Anxiety/ Depression Scale	Parent-reported symptoms of depression and anxiety	50 ± 10	Worse Functioning
Child Behavior Checklist (CBCL): Externalizing Problems	Parent-reported symptoms of externalizing behavior (e.g., aggression, conduct problems)	50 ± 10	Worse Functioning
Child Behavior Checklist (CBCL): Total Problems	Overall parent-report behavior and emotion symptoms	50 ± 10	Worse Functioning
Children's Depression Inventory: Total Score	Child's report of depression symptoms	50 ± 10	Worse Functioning
Behavior Rating Inventory of Executive Function (BRIEF): Behavioral Regulation Index	Parent-reported behavioral self-regulation (e.g., impulse control, emotional control)	50 ± 10	Worse Functioning
Behavior Rating Inventory of Executive Function (BRIEF): Metacognition Index	Parent-reported mental self-regulation (e.g., organization, planning, self-initiation)	50 ± 10	Worse Functioning
Behavior Rating Inventory of Executive Function (BRIEF): Global Executive Composite	Overall self-regulation	50 ± 10	Worse Functioning

See the text for citations related to each measure.

*Wechsler Intelligence Scales = Wechsler Intelligence Scale for Children, 4th Ed (<17 years) and Wechsler Adult Intelligence Scale, 4th Ed (17+ years).

Table 2

Demographics of study population*

Variable	Category	cSLE (n=40)	Controls (n=40)	p-value
Age at enrollment (years)		14.8 ± 2.3	13.9 ± 3.2	***0.03***
Gender	Female	85.0%	85.0%	1.0
Ethnicity	White	30.0%	32.5%	0.98
	Black	45.0%	47.5%	
	Hispanic	17.5%	15.0%	
	Asian and other	7.5%	5%	
Grade Level	Elementary School (4-6)	20.0%	20.0%	1.0
	Middle School (7-8)	17.5%	17.5%	
	High School (9-12)	62.5%	62.5%	
Maternal education level	No High School Diploma	7.5%	10.0%	0.7
	Completed High School Diploma	30.0%	37.5%	
	Education Beyond High School	62.5%	52.5%	
Family Income	< $25,000	20.0%	15.8%	0.81
	$26-$50,000	35.0%	34.2%	
	$51-$75,000	20.0%	28.9%	
	>$75,000	25.0%	21.1%	
cSLE Duration (months)		23.7 ± 23.1		
Physician assessment of disease activity†		2.4 ± 2.0		
Disease activity (SLEDAI-2k)‡		4.9 ± 4.4		
Disease activity (BILAG)§		3.0 ± 3.8		
Disease damage (SDI)‖		0.4 ± 0.8		
On Prednisone therapy		77.5%		
Prednisone daily dose [mg] (N=31)		19.8 ± 17.4		

*Except where indicated otherwise, values are mean ± SD; cSLE = childhood-onset systemic lupus erythematosus.

†Measured on categorical Likert scale with 0 = inactive cSLE; 10 = very active cSLE.

‡Systemic Lupus Disease Activity Index; range 0 – 104; 0 = inactive cSLE.

§British Isles Lupus Activity Group Index; A=9; B= 3; C= 1; D or E= 0; lower scores indicate lower cSLE activity.

‖Systemic Lupus Collaborating Clinics/American College of Rheumatology damage index.

Table 3

Group comparisons for cognitive, behavioral, emotional, and executive functioning indices*

Variable	cSLE	Controls	p-value	
			cSLE vs Controls†	cSLE vs Population Norms‡
WASI Full Scale IQ	101.0 ± 11.6	98.6 ± 12.6	0.24	0.62
Wechsler Working Memory Index	90.4 ± 20.0	94.3 ± 13.3	0.27	***<0.01***
Wechsler Processing Speed Index	94.3 ± 21.2	100.0 ± 13.0	0.09	***0.02***
WRAML-II Screening Index	102.8 ± 14.1	100.2 ± 14.0	0.37	0.23
WJ-III Letter-Word Identification	96.9 ± 10.4	96.3 ± 10.6	0.74	0.20
WJ-III Calculation	96.8 ± 14.5	94.2 ± 15.6	0.31	0.20
CPT-II Omissions	52.6 ± 13.8	55.8 ± 17.3	0.37	0.10
CPT-II Commissions	48.5 ± 7.4	50.4 ± 10.3	0.35	0.34
CPT-II Hit Reaction Time Standard Error	48.6 ± 10.7	49.6 ± 10.0	0.64	0.36
CBCL Anxiety/Depression Scale	52.2 ± 4.0	52.5 ± 4.0	0.71	0.17
CBCL Externalizing Problems	46.0 ± 8.0	47.1 ± 8.6	0.49	**0.01**
CBCL Total Problems	48.3 ± 10.0	47.2 ± 8.3	0.54	0.28
CDI Total Score	43.8 ± 7.7	44.3 ± 8.0	0.76	***<0.01***
BRIEF Behavioral Regulation Index	46.4 ± 7.0	47.6 ± 7.6	0.44	***0.02***
BRIEF Metacognition Index	49.0 ± 10.0	48.0 ± 7.4	0.59	0.54
BRIEF Global Executive Composite	47.8 ± 8.5	47.6 ± 7.2	0.88	0.16

WASI = Wechsler Abbreviated Scale of Intelligence; Wechsler = Wechsler Intelligence Scale for Children, 4th Ed (<17 years) and Wechsler Adult Intelligence Scale, 4th Ed (17+ years); WRAML-II = Wide Range Assessment of Memory and Learning, 2nd Ed; WJ-III = Woodcock-Johnson Tests of Achievement, 3rd Ed; CPT-II = Conners' Continuous Performance Test, 2nd Ed. BRIEF = Behavior Rating Inventory of Executive Function; CBCL = Child Behavior Checklist; CDI = Children's Depression Inventory. See Table 1 and text for further detail about psychometric variables.

*All values are mean ± SD; cSLE = childhood-onset systemic lupus erythematosus.

†Paired-samples t-test

‡Single-sample z-test

Table 4

Psychometric correlates of school functioning in cSLE, controls, and entire study population

Variable	cSLE	Controls	Combined Sample
WASI Full Scale IQ	0.17	0.31	0.19
Wechsler Working Memory Index	0.27	0.23	***0.27****
Wechsler Processing Speed Index	0.20	0.31	***0.25****
WRAML-II Screening Index	0.04	0.07	0.04
WJ-III Letter-Word Identification	***0.48*****	***0.33****	***0.40*****
WJ-III Calculation	***0.42*****	***0.37****	***0.37****
CPT-II Omissions	-0.02	-0.06	-0.01
CPT-II Commissions	-0.10	-0.23	-0.13
CPT-II Hit Reaction Time Standard Error	-0.04	0.05	0.00
CBCL Anxiety/Depression Scale	-0.24	-0.30	***-0.23****
CBCL Externalizing Problems	-0.14	-0.07	-0.09
CBCL Total Problems	-0.26	-0.25	***-0.26****
CDI Total Score	-0.17	-0.31	-0.20
BRIEF Behavioral Regulation Index	-0.16	-0.28	-0.17
BRIEF Metacognition Index	***-0.54*****	-0.19	***-0.44*****
BRIEF Global Executive Composite	***-0.46*****	-0.28	***-0.40*****

All values are Pearson correlations; cSLE = childhood-onset systemic lupus erythematosus.

Although some of the correlations superficially differed across the cSLE and Control groups, none of these differences were statistically significant (see text).

See legend for Table 3 for variable names.

* $p < .05$

** $p < .005$

Table 5

Disease-related correlates of school functioning in cSLE.

Variable	
SLE duration [months]	0.10
Physician assessment of disease activity	-0.18
Disease activity (SLEDAI)	***-0.55*** **
Disease activity (BILAG)	***-0.54*** **
Disease damage (SDI)	-0.22
Prednisone daily dose [mg]	***-0.40*** *

All values are Pearson correlations

cSLE = childhood-onset systemic lupus erythematosus, SLEDAI = Systemic Lupus Disease Activity Index; BILAG = British Isles Lupus Activity Group Index; SDI = Systemic Lupus Collaborating Clinics/American College of Rheumatology Damage index.

* $p < .05$

** $p < .005$