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Cognitive dysfunction in patients with childhood-onset systemic lupus erythematosus may impact treatment

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Abstract

Background Cognitive dysfunction (CD) is a widespread manifestation in adult systemic lupus erythematosus (SLE) patients, but this subject is rarely examined in patients with childhood-onset SLE (cSLE). This study aimed to assess the frequency of CD, its associations with lupus clinical manifestations and its impact on the health-related quality of life (HRQL) in young adult cSLE patients.

Methods We evaluated 39 cSLE patients older than 18 years. They underwent a rheumatologic evaluation and extensive neuropsychological assessment, encompassing all cognitive domains described by the American College of Rheumatology. HRQL was assessed with the WHOOQOL-BREEF, General Activities of Daily Living Scale (GADL) and Systemic Lupus Erythematosus-specific quality-of-life instrument (SLEQOL). The activity of SLE was evaluated with the modified sle disease activity index (sledai-2k).

Results Impairment in at least one cognitive domain was found in 35 (87.2%) patients. The most compromised domains were attention (64.1%), memory (46.2%), and executive functions (38.5%). Patients with cognitive impairment were older, had more accumulated damage and had worse socioeconomic status. Regarding the association between cognitive dysfunction and HRQL, memory impairment was correlated with worse environmental perception and a worse relationship with the treatment.

Conclusion In this study, the frequency of CD in cSLE patients was as high as that in the adult SLE population. CD can significantly impact the response of cSLE patients to treatment, justifying preventive measures in the care of this population.

Keywords Lupus erythematosus, systemic, Young Adult, Child, Cognitive dysfunction, Quality of life, Memory

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Background

Neuropsychiatric manifestations are common in adult patients with SLE. In 1999, the American College of Rheumatology published case definitions for 19 different neuropsychiatric SLE manifestations [1], which were revised by Ainiala el al. [2] in 2001. Cognitive dysfunction (CD) is one of the most common SLE manifestation and may occur in the absence of active systemic SLE disease and other major neuropsychiatric events [3]. CD is defined as a significant deficit in any of the following cognitive domains: simple or complex attention, reasoning, executive skills, memory, visual-spatial processing, language and psychomotor speed [1]. It is considered a major source of morbidity and decreased quality of life [4].

Childhood-onset systemic lupus erythematosus (cSLE) is a systemic autoimmune disease with a remitting-relapsing course for which symptoms begin prior 18 years of age. cSLE encompasses 15–20% of all lupus patients and differs from adult SLE in disease expression activity and severity, and it is associated physiological, developmental, and psychosocial issues [5, 6].

Although described as more severe [6], neuropsychiatric involvement (NPSLE) occurs at similar levels in cSLE and adult SLE patients [7]. The incidence of cognitive dysfunction is difficult to ascertain in pediatric patients because few studies have been performed. However, in adult SLE, NPSLE has been much more extensively studied [8]. The overall prevalence of cognitive dysfunction (CD) in adult SLE has been reported to be 38% (3 to 83%) [9] and 32.9% (16.1–55.7%) in cSLE [10]. This wide variation is probably secondary to heterogeneity in patients' demographic characteristics and comorbidities, the lack of standardization in the definitions, and the use of different metrics to determine these factors [9].

As part of the brain maturation process, cognitive skills advance steadily during childhood. Inflammatory brain diseases can disrupt the critical, normal maturational processes that occur from childhood through adolescence. However, whether the plasticity exhibited by young brains after central nervous system (CNS) inflammation can translate into a type of "catch-up brain growth" for pediatric patients or whether an injury during the window of growth and maturation is more severe than an injury to the fully developed adult brain is unclear [8, 11].

In addition to disease activity and damage related to the disease itself or the treatment, health-related quality of life (HRQL) is a relevant measure in SLE patients. Understanding the effects of SLE on physical, social, and psychological aspects is crucial to patient management. Previous studies have shown that CD is a common clinical manifestation that considerably impacts HRQL in patients with SLE [3, 4].

Therefore, this study aimed to evaluate the prevalence of CD, its associations with lupus clinical activity and damage, and its effect on HRQL in a group of young adult cSLE patients.

These data are limited in the literature but essential to improve knowledge about the disease and provide better care for these patients.

Methods

In this cross-sectional study, we evaluated 39 cSLE patients older than 18 years undergoing regular follow-up at the rheumatology service consecutively from August 2013 to September 2015. The cSLE diagnosis was based on the Systemic Lupus International Collaborating Clinics classification criteria (SLICC) [12]. Pregnant and lactating women were excluded. All individuals signed the informed consent approved by the institutional Ethics Committee (CAAE: 02698712.5.0000.5149). All subjects underwent a clinical evaluation, which included a rheumatologic and psychological assessment. Medical history, including laboratory tests results were obtained from medical clinical records of follow-up consultations in our walk-in clinic; no further laboratory tests other than routine ones were performed for this study.

The neuropsychological assessment was carried out face to face by a single trained neuropsychologist for all included patients. It consisted of a neurocognitive battery for the evaluation of attention (five digits test), psychomotor speed (nine-hole test), memory (Rey Auditory-Verbal Learning Test (RAVLT)), executive function (EF) (Frontal Assessment Battery (FAB)), visual-spatial processing (Rey Figure Test), language (TN_LIN) [13, 14] and reasoning/problem solving (IQ (Vienna Matrices)) [15]. Patients were considered to have CD if the score of each test was 2.0 or more standard deviations below the normative score corrected for age, education, sex, and ethnic group, when necessary. In parallel, as reported by Mikdashi et al. in the evaluation of the three key domains (attention, memory, and psychomotor speed), we classified CD as focal if one of these domains was affected and multifocal when measures spanning two or more domains were compromised [1, 16].

Clinical activity was assessed with the SLE Disease Activity Index (SLEDAI 2 K) [17] Irreversible cumulative damage caused by SLE or by complications from treatment was measured using the Systemic Lupus International Collaborative Clinics/American College of Rheumatology Damage Index (SLICC/ACR – DI) [18].

HRQL was assessed with the WHOQOL-BREEF [19], General Activities of Daily Living Scale (GADL) [20] and SLEQOL [21]. The stratification of socioeconomic status was assessed with the Brazil Criterion [22].

Table 1 Demographic and clinical characteristics for 39 patients with childhood-onset systemic lupus erythematosus

Characteristic		Value
Sex		31 female / 8 male
Age at diagnosis (years)		14.58 (9.49–17.84)
Age at evaluation (years)		21.47 (18.05–35.71)
Disease duration (years)		8.08 (1.74–23.79)
Years of education		11.0 (6–17)
History of NPSLE		8 (20.5%)
Anti dsDNA (cumulated)		21(53.8%)
SLEDAI 2 K		2.0 (0–16)
SLICC/ACR - DI		0 (0–5)
Cumulative prednisone dose (mg)		35.720.0(9,279.0–127,530.0)
Current prednisone dose (mg)		7.5 (0–60)
Brazil Criterion	A2	(5.1%)
	B1	(7.7%)
	B2	(38.5%)
	C1	(28.2%)
	C2	(17.9%)
	D	(2.6%)

(Absolute value(N), %, median, maximum and minimum values)

NPSLE: Neuropsychiatric Systemic Lupus

dsDNA: double-stranded DNA

SLEDAI 2 K: Systemic Lupus Erythematosus Disease Activity Index;

SLICC/ACR-DI: Systemic Lupus International Collaborative Clinics / American College of Rheumatology Damage Index

The modified ACR case definition for neuropsychiatric lupus syndrome [1, 2] was used to define NPSLE in this study.

Data were analyzed using SPSS 20.0 (Statistical Package for Social Sciences, IBM Corporation Software Group, USA), and significance was defined as a p value <0.05. The Shapiro–Wilk test was used to analyze the distribution of the data. Normally distributed variables were summarized using the mean and standard deviation (SD), and nonnormally distributed variables were reported as the median and range. Univariate comparisons between nominal variables were calculated using the chi-square (x^2) test or Fisher's test where appropriate. Two-tailed P values less than or equal to 0.05 were considered significant. Student's T tests and Mann–Whitney U tests were used to compare the medians. For the correlation between continuous variables, Pearson or Spearman tests were used.

Results

A total of 39 patients (31 women) were included. Their demographic and clinical characteristics are displayed in Table 1.

Impairment in at least one neuropsychological domain was identified in 35 (87.2%) patients. The most compromised domains were attention (64.1%), memory (46.2%), and executive functions (38.5%). Patients were classified as having focal cognitive impairment in 48.7% of cases and multifocal in 33.3%. (Table 2).

Table 2 Frequency of cognitive impairment in each domain and classification by Mikdashi [15]

Variable		N = 39 (%)
At least one cognitive domain impaired		35 (87.2%)
Attention		25 (64.1%)
Executive Function		15 (38.5%)
Memory		18 (46.2%)
Psychomotor Speed		7 (17.9%)
Visual-spatial processing		5 (12.8%)
Language		2 (5.1%)
Reasoning		1 (2.6%)
Key domain impairment		32 (82.1%)
	Normal	7 (17.9%)
	Focal	19 (48.7%)
	Multifocal	13 (33.3%)

Key domain: attention memory, psychomotor speed

CD was not associated with a history of NPSLE (p=0.732), age at diagnosis of cSLE (p=0.556), disease duration (p=0.933), cumulative prednisone dose (p=0.401), years of formal schooling (p=0.217), the Brazil Criterion (p=0.105) or median scores of SLEDAI 2 K (p=0.860).

Executive functions were compromised in patients with more accumulated damage [1 (0–5) vs. 0 (0–4), p=0.028] and in those with fewer years of schooling [11.0(7–11) vs. 11.0(6–17)] P=0.042. The median age was higher in patients with memory impairment than in those with normal memory [23.2 (19.8–31.5) vs. 19.8 (18.1–35.7), p=0.043].

CD patients showed worse performance related to the perception of the environment, evaluated by the WHOOQOL-BREEF, which includes aspects such as opportunities and the ability to acquire new information [59.4(40.63–87.7) vs73.4(68.75–87.5), p=0.032].

Patients with impaired memory had worse environmental perception (p=0.030) and a worse relationship with treatment (p=0.010) than those with normal memory. According to the GADL, patients with visual-spatial processing (p=0.008) and language (p=0.000) impairments were more dependent (Table 3).

Older patients (p=0.007) had a poorer perception of their treatment issues. Based on the Brazil Criterion, worse socioeconomic status was associated with impaired memory [20(10–34) vs. 24(15–39), p=0.048] and executive function [20 (10–33) vs. 24 (16–39), p=0.016]. Patients with an unfavorable socioeconomic status had a poorer perception of their treatment issues (p=0.036). Those with better socioeconomic situations

Table 3 Comparative analysis of health-related quality of life in childhood-onset systemic lupus erythematosus patients with and without cognitive dysfunction (n = 39)

		Memory			Visual-spatial processing			Language		
		Yes	No	*p*	Yes	No	*p*	Yes	No	*p*
WHOQOL-BEEF	Physical health	**62.48** (35.7–75.0)	**64.29** (42.9–82.1)	**0.350**	**73.57** 50.0–75.0	**64.26** 35.7–82.1	**0.813**	**51.8** 50.0-53.6	**64.3** 35.7–82.1	**0.117**
	Environment	**57.85** 40.6–84.4	**68.75** 72.8–87.5	**0.030**	**62.50** 46.9–71.9	**60.94** 40.6–87.5	**0.962**	53.1 46.9–59.4	62.5 40.63–87.5	**0.237**
	Psychological	**70.83** 41.7–83.3	**66.67** 41.7–79.2	**0.756**	**70.83** 50.0-79.2	**66.67** 41.7–83.3	**0.336**	54.2 50.0-58.3	70.8 41.7–83.3	**0.095**
	Social relationship	**75.0** 41.7–100.0	**83.33** 33.3–100.0	**0.213**	**75.0** 66.7–100.0	**75.0** 33.30–100.0	**0.924**	75.0 66.7–83.3	75.0 33.3–100.0	**0.796**
SLEQOL	Treatment	**11.0** 4.0–18.0	**6.0** 4.0–13.0	**0.010**	**8.0** 4.0–12.0	**9.5** 4.0–18.0	**0.329**	**8.0** 4–12	**9.0** 4–18	**0.720**
	Physical function	**8.0** 6.0–28.0	**8.0** 6.0–29.0	**0.798**	**9.0** 6.0–28.0	**8.0** 6.0–29.0	**0.330**	**17.0** 6–28	**8.0** 6–29	**0.713**
	Symptoms	**15.5** 8.0–32.0	**12.0** 8.0–23.0	**0.211**	**16.0** 8.0–21.0	**12.5** 8.0–32.0	**0.601**	**18.5** 16.0–21.0	**13.0** 8.0–32.0	**0.282**
	Mood	**9.0** 4.0–26.0	**6.0** 4.0–19.0	**0.310**	**10.0** 4.0–12.0	**7.0** 4.0–26.0	**0.905**	**8.0** 4.0–12.0	**7.0** 4.0–24.0	**0.694**
	Self-image	**15.5** 9.0–48.0	**13.0** 9.0–27.0	**0.267**	**15.0** 12.0–29.0	**15.0** 9.0–48.0	**0.687**	**20.0** 11.0–29.0	**15.0** 9.0–48.0	**0.803**
	Occupational activity	**19.0** 9.0–52.0	**15.0** 9.0–39.0	**0.539**	**25.0** 9.0–43.0	**15.0** 9.0–52.0	**0.245**	**29.0** 15.0–43.0	**17.0** 9.0–52.0	**0.334**
	GADL	**26.0** 14–26	**26.0** 24–26	**0.851**	**23.4** 14–26	**25.93** 24–26	**0.008**	**19.0** 14–24	**26.0** 25–26	**0.000**

SLEQUOL - Systemic Lupus Erythematosus-specific quality-of-life instrument

GADL: General Activities of Daily Living Scale;

Table 4 Correlations between health-related quality of life scores and clinical and demographic characteristics (N = 39)

	Domains	Current Age		Brazil Criterion		SLEDAI 2 K		SLICC/ACR-DI	
		r	*p*	*r*	*p*	*r*	*p*	*r*	*p*
WHOQOL BREF	Physical health	-0.011	0.948	0.236	0.149	-0.082	0.618	-0.008	0.959
	Environment	-0.256	0.116	0.498	0.001	0.077	0.642	-0.032	0.849
	Psychological	-0.870	0.559	0.233	0.153	0.076	0.645	0.007	0.966
	Social relationship	-0.183	0.264	0.100	0.547	0.101	0.540	0.008	0.963
SLEQOL	Treatment	0.450	0.007	-0.355	0.036	0.008	0.963	-0.059	0.736
	Physical function	0.018	0.918	-0.089	0.612	-0.130	0.457	0.086	0.624
	Symptoms	0.214	0.216	-0.234	0.176	-0.213	0.219	-0.014	0.939
	Mood	0.224	0.196	-0.149	0.392	-0.173	0.322	-0.068	0.696
	Self-image	0.179	0.303	-0.041	0.816	0.004	0.984	-0.076	0.665
	Occupational activity	0.102	0.559	-0.115	0.510	-0.028	0.873	-0.080	0.649
	GADL	-0.245	0.133	0.014	0.930	0.226	0.166	-0.149	0.365

W: WHOQOL-BREEF; SLEQOL; SLEDAI 2 K: SLE Disease Activity Index; SLICC/ACR - DI: Systemic Lupus International Collaborative Clinics / American College of Rheumatology Damage Index

were more satisfied with their environmental status (p = 0.001). These data are described in Table 4.

We did not find an association between CD and the anti dsDNA antibody (p = 0.215).

Discussion

The present study evaluated the prevalence of CD, encompassing all cognitive domains described by the ACR and its impact on HRQL, in a group of young adults with cSLE. We identified impairment in at least one neuropsychological domain in 87.2% of the patients and 82.1% when only the key domains (attention, memory and psychomotor speed) described by Mikdashi [16] were analyzed. These global data are similar to those found in the adult population, as well as for each specific domain [9, 23, 24].

Despite being very young, the older patients evidenced worse memory and inferior perception of treatment issues to SLEQOL. Remembering to take the medication and remembering the scheduled appointments and exams are items questioned in this domain. Memory impairment may hinder all actions involved in

the treatment of lupus patients and might be one of the critical determinants of the lack of treatment adherence in these patients [25]. Patients, who are now adults and assuming responsibility for treatment, may suffer a more significant impact.

Those who are socioeconomically disadvantaged showed worse memory, executive functions, and perception of environment and the treatment. Previous studies have provided consistent evidence to support that the global childhood stratification of socioeconomic status as any of its specific components are associated with levels of cognition—both in terms of memory and executive function. However, the mechanisms underlying the stratification of socioeconomic status differences in specific neurocognitive functions at the behavioral or neurobiological levels have not been completely elucidated to date [26, 27].

Impairment in visual spatial processing and language domains negatively impacts the patients' activities of daily living when assessed by GALD. This test provides a synthetic tool to evaluate the activities of daily living. The ability to communicate verbally is known to be fundamental to an individual's development and well-being [28]. Visual-spatial processing is the ability to understand where objects are in space, which includes the perception of body parts and being able to tell how far objects are from you and from each other. de Paula et al. [29] describe visual-spatial processing impairment as a significant predictor of the ability to go out alone and use transportation, which clearly impacts the individual assessment of quality of life, and it has a negative impact not only on the patients' independence but also particularly on the performance of the activities of daily living [30]. Because the impairment of cognitive functions is part of the assessment of damage associated with SLE, patients with higher SLICC/ACR – DI scores can be expected manifest a higher frequency of executive function impairment, as found in this study. Patients with the worst performance in the assessment of executive functions had fewer years of formal schooling. Patients with more years of education were less likely to have CD; and education, as measured by the number of years of formal schooling, may have beneficial effects on executive function, as described by Cotrena et al. [31]. However, experiencing learning difficulties is a known cause of school dropout [32].

Knight et al. [5] described a group of young patients with cSLE and mixed connective tissue disease. These patients had established peer support and displayed a positive illness identity. They described themselves as being in control of their illness with minimal impact on daily activities, functioning, and sense of self. These findings support our results. The apparent small impact of CD in most aspects of the HRQL may be due to the good social relationships of the studied patients, as evaluated in this domain in the WHOQOL-BREEF.

CD is a significant challenge in SLE patients. Studies of adult-onset SLE noted the relevance of this problem based on the patients' HRQL [33]. Ceccarelli et al. [23] reported deficits in attention in 10%, memory in 20%, and executive function in 20% of patients. These results were similar to those reported by Maciel et al., who revealed impairment in executive functions in 20.4% of patients [24]. Although some authors have described an effect on verbal fluency [16], quantitative rates have not been reported. We found that at least one cognitive domain was involved in 87.2% of the patients, and this frequency is greater than that previously reported, including a study conducted at the same hospital of adult-onset SLE patients, in which the overall incidence of CD was 72.2% [24]. We recognize that the critical cognitive maturation period from late childhood through adolescence and into young adulthood coincides with the pediatric age spike for SLE onset. The burden of chronic illness during adolescence, a time of critical psychosocial development, is reflected in these higher incidences of CD in all cognitive domains [11].

We did not find an association between CD and the anti dsDNA antibody. Ahn et al. asserts that absence of anti-dsDNA antibody at SLE diagnosis are risk factors for development of NPSLE [34]. As previously reported, most studies have found no correlation between CD and disease activity or damage [16, 35], and our study also found no correlation, except for EF and SLICC/ACR/DI. Although corticosteroids reportedly have complex and underappreciated adverse effects on psychological health [36], we did not find a correlation between cumulative prednisone dose and CD or any aspect of the WHOQOL-BREEF or SLEQOL. Preliminary studies show that disease activity does not correlate with patients' HRQL [37], which is consistent with our description of the lack of correlation between HRQL and SLEDAI scores.

We did not find a correlation between CD and NPSLE history as did others authors [3, 38–42]. It is worth highlighting that such results were obtained in spite of an active search for cognitive dysfunction in our sample of 39 patients with cSLE, performed by a single trained neuropsychologist in individual interviews. Also, this result may be due to the low incidence of history of NPSLE in our sample (20.5%). This low incidence, in its turn, may be due to the fact that our data were the result of analysis of medical records of routine consultations that might have overlooked mild and less severe manifestations of NPSLE, unlike severe ones such as psychotic episodes, convulsive crises and neuromyelitis, which are always inquired and properly scrutinized.

To the best of our knowledge, this study is the first to examine all cognitive domains described by the ACR

associated with the use of three scores to access their HRQL in young adult cSLE patients. The use of categorical classification (i.e., impaired/not impaired) simplifies the evaluation of the commonly observed cognitive deficits in SLE and cSLE. An essential limitation of the present study is the small sample size, which potentially impacted the small correlation observed between DC and the HRLQ scores. Another limitation is that most patients have a fluctuating and evanescent pattern of DC, and we may have overestimated or underestimated the frequencies of DC in our patients and its correlations with HRQL.

Table 5 describes the main studies on cognitive dysfunction cited in the text.

Table 5 Texts on cognitive disorder in SLE used as references and its results

Authors	N	Main Results
(Ahn, Kim et al. 2018)	1121 SLE patients	• 429 patients(38.3%) had NPSLE manifestations according to ACR criteria and 216 (19.3%) by Ainiala criteria. • Higher SLEDAI, antiphospholipid antibody positivity, absence of anti-dsDNA antibody at SLE diagnosis, and fewer years of education are risk factors for development of NPSLE. Presence of NPSLE, especially focal CNS NPSLE, increased the risk of mortality in SLE patients
(Ceccarelli, Perricone et al. 2018)	43 SLE Patients	• CD: 20.9% at first evaluation (T0) and 13.9% 10 years later (T1) • CD improved in the majority of the patients. Furthermore, we observed an improvement of the overall cognitive functions.
(Dorman, Micelli et al. 2017)	84 SLE patients	• Working memory: 42%; visual memory: 22%; processing speed: 36%; viso-construction: 20%; semantic verbal fluency: 21% • They observed a statistically significant association between the higher value of SLEDAI and working memory impairment and a higher value of SLICC and viso-construction and semantic verbal fluency impairment. The association observed in SLE patients between disease activity or damage and some cognitive domains may be involving different pathophysiological brain mechanisms of different areas with different degrees of severity and vulnerability
(Hanly, Fisk et al. 1992)	70 SLE patients	• Cognitive impairment is increased in patients with SLE. • It may occur independently of clinically overt NP-SLE • It is more common in patients with active disease who are receiving corticosteroids.
(Langensee, Mårtensson et al. 2022)	91 female participants (33 NPSLE, 29 non-NPSLE, 29 healthy controls)	• Cognitive performance is affected in both non-NPSLE and NPSLE patients
(Leslie and Crowe 2018)	Systematic review / meta-analyse	• Medium-sized deficits were observed in NPSLE patients relative to healthy controls across the domains of: complex attention, delayed verbal memory, language and verbal reasoning (with small ornon-significant differences observed in non-NPSLE patients relative to healthy controls)
(Maciel, Ferreira et al. 2016)	54 SLE patients	• The overall frequency of cognitive dysfunction was 72.2% • Executive functions compromised in 20.4%
(Monastero, Bettini et al. 2001)	75 SLE female patients	• Cognitive impairment was identified in 14 (26.9%) and in 12 (52.2%) of subjects with nSLE and NPSLE, respectively. • Cognitive impairment occurs frequently in both nSLE and NPSLE subjects
(Rayes, Tani et al. 2018)	Systematic review / meta-analyse	• Wide prevalence of CD ranging between 3% and 81%
(Sabbadini, Manfredi et al. 1999)	179 SLE patients	• 114 SLE patients who had never received a diagnosis of neuropsychiatric lupus (neverNPSLE) were studied and compared to 65 SLE patients with known neuropsychiatric involvement (NPSLE) • Most features of CNS involvement were present in 114 `never-NPSLE' patients who had no neuropsychiatric manifestations either at the time of the study or in their clinical history, analyzed by: (i) assessment of superior functions (neurocognitive tests and psychiatric interviews);
(Santos, Nascimento et al. 2021)	Systematic review / meta-analyse	• The results for each syndrome: headache (52.2%), seizure disorders (48.6%), cognitive dysfunction (32.9%), mood disorder (28.3%), psychosis (22.7%), cerebrovascular disease (19.5%), acute confusional state (15.7%), movement disorder (9.4%), anxiety disorder (7.2%), aseptic meningitis (5.1%), mononeuropathy single/ multiplex (4.9%), myelopathy (4.2%), demyelinating syndrome (3.2%), cranial neuropathy (2.7%), polyneuropathy (2.6%), Guillain-Barré syndrome (2.5%), autonomic disorder (1.9%), plexopathy (1.3%), and myasthenia gravis (1.3%).
(Seet, Allameen et al. 2021)	Review	• CD has a substantial impact on the HRQoL of patients with SLE. • The current standard of practice encompasses eliciting a good clinical history of impaired functioning, supported by objective assessment via comprehensive neuropsychological testing.
(Yue, Gurung et al. 2020)	78 SLE patients	• Total prevalence: 67.9% • CD was not associated with disease activity • Serum anti NMDAR antibodt can be used as a predictor for SLE related CD • Domains affected: delayed recall (80.5%), abstract generalization (79.2%). Verbal repetition and fluency (76.6%)

Conclusions

In this sample, a group of young adults with a diagnosis of cSLE showed a high prevalence of CD. Although the patients were very young, their cognitive functions progressively worsened and a greater difficulty in conducting their treatment was noted as they aged, especially in those with a worse SES. A multidisciplinary approach that considers the individual variability of the clinical manifestations of the disease may help to improve the early detection of CD, given that these clinical manifestations are responsible for decreased treatment adherence with a subsequently increased risk of comorbidities. Physicians across all specialties involved in the care of SLE patients should be aware of the significant incidence of CD while helping patients cope with the disease and its disabling consequences. Follow-up studies that evaluate the prevalence and evolution of CD are vital in this population.

List of Abbreviations

CD	Cognitive dysfunction
cSLE	Childhood-onset systemic lupus erythematosus
EF	Executive functions
FAB	Frontal Assessment Battery
GADL	General Activities of Daily Living Scale
HRQL	Health-related quality of life
NPSLE	Neuropsychiatric Systemic Lupus Erythematosus
RAVLT	Rey Auditory-Verbal Learning Test
SLE	Systemic lupus erythematosus
SLEQOL	Systemic Lupus Erythematosus-specific quality-of-life instrument
SLEDAI-2k	Modified Systemic Lupus Erythematosus Disease Activity Index
SLICC	Systemic Lupus International Collaborating Clinics classification criteria
SLICC/ACR-DI	Systemic Lupus International Collaborative Clinics/American College of Rheumatology Damage Index
SES	Socioeconomic Status
WHOQOL	World Health Organization Quality of Life instrument
WHOQOL-BREF	World Health Organization Quality of Life instrument - short version

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

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Authors' contributions

Conception and design: FPSTS, GAF, HC; Data collection: FPST, KP, SCS; Data Processing and Statistical analysis and interpretation: FPST, GAF, JJP; Literature review: FPST. Writing: FPSTS. Critical review: GAF, HC, JJD. All authors read and approved the final manuscript.

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Data Availability

data are available for conference, if necessary.

Code Availability

Data analysis was performed using SPSS 20.0 (Statistical Package for Social Sciences, IBM Corporation Software Group, USA), provided by Post graduation Program in Molecular Medicine, Universidade Federal de Minas Gerais (UFMG), Belo Horizonte, Minas Gerais, Brazil.

Declarations

Ethics approval

The research was approved by University (UFMG) Ethics Committee (CAAE: 02698712.5.0000.5149), and all patients have signed the approved informed consent.

Consent to participate

All patients signed the informed consent.

Consent for publication

All authors agree with the submission of the work to *Advances in Rheumatology* and agree with the rules of the Journal.

Conflicts of interest/Competing interests

The authors declare no potential conflicts of interest with respect to the research authorship, and/or publication of this article.

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