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ORIGINAL RESEARCH

Multimodal neurophysiological and psychometric evaluation among patients with systemic lupus erythematosus

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Objective: To determine some of the neuropsychiatric manifestations of systemic lupus erythematosus (SLE) by applying multimodal neurophysiological and psychometric studies.

Patients and methods: Twenty-six SLE patients were evaluated for neurological and psychiatric disorders and compared with 26 healthy controls matched for age, sex, education, and social class. The severity of SLE disease was assessed. Each subject was subjected to the following examinations: laboratory, neurophysiology, magnetic resonance imaging of the brain, transcranial duplex, Modified Mini-mental State Examination, Cognitive Assessment Scale Inventory, Hamilton Depression Scale, and Hamilton Anxiety Scale.

Results: The mean age of subjects was 25.9 ± 8.9 years. The most prevalent neurological manifestations were (in order of frequency) anxiety in 17 cases (65.4%), depression in 15 cases (57.7%), headache in 10 cases (38.5%), peripheral neuropathy in 7 cases (26.9%), seizures in 6 cases (23.1%), psychosis in 5 cases (19.2%), dementia in 4 cases (15.4%), radiculopathy in 4 cases (15.4%), myositis in 3 cases (11.5%), and stroke in 2 cases (7.7%). There was a significant affection in amplitude of the ulnar nerve, cognitive function impairment, and electroencephalography changes. There was a significant increased mean velocity and decreased Pulsatility Index of the most studied intracranial vessels in the patients.

Conclusion: The use of multimodal neurophysiological, transcranial duplex, and psychometric scales increases the sensitivity for detecting nervous system involvement.

Keywords: SLE, SLEDAI, cognitive function, depression, anxiety, neurological disorders

Introduction

Systemic lupus erythematosus (SLE) is a multisystem disease with a spectrum of clinical manifestations and a variable course characterized by exacerbation and remission.[1] In the course of SLE, a variety of neuropsychiatric disturbances is reported, with prevalence rates ranging from 17% to 75%.[2] The challenge in patients with SLE is to determine whether neuropsychiatric affection is functional due to a psychogenic basis or an organic abnormality such as dysfunction of the central or peripheral nervous system.[1] Furthermore, if the cause is organic, are those symptoms or findings due to lupus itself (either active or inactive) or to other causes? A previous report[3] on the prevalence of neuropsychiatric affection from most to least prevalent is as follows: cognitive dysfunction, headache, mood disorder, cerebrovascular changes within intracranial vessels, seizures, polyneuropathy, anxiety, and psychosis.

The use of multimodal neuropsychiatric evaluations is essential for diagnosis of early affection. Electroencephalography (EEG) may be helpful to confirm changes or diffuse encephalopathy.[1] Electromyography (EMG) and nerve conduction studies

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(NCS) provide useful data in the clinical assessment of peripheral complications of SLE.[4] Transcranial duplex (TCD) confirms that subclinical cerebrovascular changes affect intracranial vessels in SLE.[4] The aim of the present study was to characterize the potential neurological involvement of unselected SLE patients and index of disease activity.

Patients and methods

Twenty-six SLE patients (24 females and 2 males) with ages ranging from 10 years to 40 years were selected at the outpatient clinic wards of Assiut and Al-Azhar (Assiut) University Hospitals, Egypt. All patients met the diagnostic criteria of SLE.[5] Rheumatologic evaluation was completed using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI).[6] Exclusion criteria included: i) age below 10 years or more than 40 years; ii) pre-existing clinical cardiovascular or cerebrovascular events (angina, myocardial infarction, transient ischemic attack, or stroke); iii) other systemic diseases (such as renal, liver, or endocrinal diseases) or taking drugs known to have central nervous system effects; or iv) cancer discovered in the previous 5 years. Medications at the time of the study included non-steroidal anti-inflammatory drugs, prednisone (10–20 mg/d) in all cases and disease-modifying anti-rheumatic drugs (hydroxychloroquine, azathioprine, methotrexate, and cyclophosphamide).

SLEDAI measures the current status of SLE disease activity according to clinical and laboratory manifestations. SLE disease activity is defined as the reversible manifestations of the underlying inflammatory process.[6] SLEDAI consists of 24 weighted attributes, which are grouped into 9 domains, called organ systems (weighting in parenthesis): central nervous system (8), vascular (8), renal (4), musculoskeletal (4), serosal (2), dermal (2), immunologic (2), constitutional (1), and hematologic (1). SLEDAI is a reliable and valid instrument for measuring the clinical state of SLE patients.[6,7]

Twenty-six healthy individuals matched for age, sex, number of education years, and socioeconomic status[8] were selected as a control group from relatives of patients. These control groups were examined and fully investigated.

The Regional Ethical Committee of Assiut University Hospitals and Al-Azhar (Assiut) approved the study. All subjects gave their written informed consent for participation.

Methods

All subjects (patients and control) were subjected to full medical, neurological, and rheumatological examination and socioeconomic status assessment.[8] Multimodal neurophysiological and psychometric tests were applied for all subjects. Venous blood was obtained from all subjects by puncturing an antecubital vein at 8 a.m. after overnight fasting. A complete blood count was performed using automated cell counter, and blood urea and serum creatinine were measured by the spectrophometeric method. Normal ranges were as follows: blood urea 30–50 mg/dL and serum creatinine <1.5 mg/dL.[9] Liver function tests were performed by a spectrophotometeric method using Stat Fax (Awareness Technology, Dubai, United Arab Emirates). Normal ranges were as follows: aspartate aminotransferase 0–35 U/L and alanine aminotranferease 0–35 U/L.[10] Fasting blood glucose was measured by spectrophotometeric method, complete urinalysis was performed by microscopic examination, and 24-hour collection of urine protein was by spectrophotometeric method. Disease activity indexes such as erythrocyte sedimentation rate using the western green tubes method were considered normal when less than 10 mm/hour.[11] Antinuclear (ANA) and anti-double-stranded DNA (anti-dsDNA) were measured using enzyme-linked immunosorbent assay method and determined in controls to exclude the presence of autoimmune diseases.

Imaging studies

All subjects underwent magnetic resonance imaging of the brain and transcranial duplex (TCD). TCD was carried out using Nicolet Bravo model 460 SNF0000001544 (Neurocare, Madison, WI) with a 2 mHz probe, which provided a direct and noninvasive assessment of subclinical atherosclerosis. TCD examinations were performed at the Department of Neurology and Psychiatry, Clinical Neurophysiology Unit, Assiut University Hospital. The right anterior cerebral artery (ACA) was assessed via transtemporal window. The depth of insonation was between 60 mm and 90 mm with subject head in a neutral position. The right middle cerebral artery (MCA) was assessed via a transtemporal window. The depth of insonation was between 30 mm and 60 mm with subject head in a neutral position. Right posterior cerebral artery (PCA) was assessed via transtemporal window. The depth of insonation was between 60 mm and 80 mm with subject head in a neutral position. Right vertebral artery (VA) was assessed via suboccipital window. The depth of insonation was between 60 mm and 90 mm with subject head in a neutral position. Right basilar artery (BA) was assessed via suboccipital window. The depth of insonation was between 80 mm and 120 mm with subject head in a neutral position. Systolic mean velocity (MV) and Pulsatility Index (PI)

were recorded as PI equal to the peak velocity minus the end-diastolic velocity divided by the MV.[12] The PI normal range is 0.5–1.1.[13]

Neurophysiologic studies

Conventional 20-minute EEG recordings were obtained using the 8-channel Nicolet Bravo model 460 SNF0000001544. The electrodes were placed on the scalp according to the International 10–20 System of Electrode Placement using bipolar and referential montages. Hyperventilation was used as a provocative test. Seizures were divided into epilepsy (chronically recurrent seizures occurring in a stereotypic pattern corresponding to anatomically focal spikes on EEG) and isolated seizures (usually corresponding to generalized slowing on EEG).

Motor nerve conduction velocity (MCV) studies were performed on the right ulnar, median, and common peroneal nerves. MCV, distal latency (DL), and amplitude of compound muscle action potential (CMAP) were measured with standard surface stimulating and recording techniques. The latency was measured from the stimulus onset to the beginning of the initial deflection of the CMAP. The MCV can be calculated by stimulating at two different points along the nerve and measuring the latency for each response. F-wave (for median, ulnar, and common peroneal nerves) was measured by putting the recording electrodes on the distal muscle innervated by the testing nerve, employing the belly-tendon method. F-wave latency was measured from the start of the stimulus to the onset of initial deflection of the F-wave with the shortest latency. The latency of the F-wave after distal stimulation is usually in the range of 23–33 milliseconds for median and ulnar nerves in normal individuals and of 50–60 milliseconds for the peroneal nerves.

An H-reflex study was measured by placing the recording electrodes on the gastrocnemius muscle and stimulating the posterior tibial nerve at the popliteal fossa. The latency was measured from the start of stimulation to the onset of the initial deflection of the H-reflex. The latency of the H-reflex is usually in the range of 25–35 milliseconds in normal individuals.

Psychometric

The Cognitive Abilities Screening Instruments (CASI) consists of 25 test items and provides quantitative assessment of attention, concentration, orientation, memories for post-knowledge and present input, language abilities, drawing and writing abilities, list-generating ability, abstract thinking, and judgment.[14] The CASI is more comprehensive than most screening tests of cognitive abilities and can be used to screen for early cognitive impairment and dementia. We considered the cutoff of CASI as that according to Ross et al,[15] which is ≤67 points for dementia. The Mini-mental State Examination (MMSE) is a widely used scale for screening for dementia.[16] Most of the subjects of the present study were illiterate. The two points testing reading and writing were excluded, and the full score was calculated as 28 instead of 30 points. The cutoff point of dementia was 21 instead of 23 points.[17] In the present study, dementia was diagnosed if the clinical presentation fulfilled criteria of dementia as well as when the subject scored ≤21 on the MMSE and ≤67 on the CASI.[18] The Hamilton Depression Scale is a widely used and reliable scale and not specific for elderly people.[19] The cutoff point of depression in this scale is ≥17, according to Michele and Bolino.[20] Numerous authors have since investigated the dimensionality of the scale and demonstrated that it is multidimensional.[19] The Hamilton Anxiety Scale lists 14 types of symptom. The total score ranges from 0 to 56. A total score of 18 or more means anxiety.[21]

Statistical analysis

The computer software package SPSS® for Windows (Version 16) (IBM, Chicago, IL, USA) was used for the data analysis. Continuous variables such as age were expressed as mean ± standard deviation, whereas categorical variables such as gender were presented as frequencies (%). The Pearson Chi-square test and independent-sample *t*-test did not assume equal variances were used. A series of Pearson correlation coefficients was used to examine SLEDAI and different variables. Significance level was set at $P \leq 0.05$.

Results

Details of demographic data, systemic examination, and laboratory data are illustrated in Tables 1 and 2. There were

Table 1 Demographic data of patients and control group

Item	Control N = 26	Cases N = 26	*P* value
Age (mean ± SD)	25.9 ± 8.9	24.9 ± 7.6	0.65
Sex			
Male (n%)	2 (7.7%)	2 (7.7%)	0.383
Female (n%)	24 (92.3%)	24 (92.3%)	
Duration of illness (mean and range/years)		4.85 (1–15 years)	
Number of education years (mean ± SD)	3.7 ± 0.55	3.8 ± 0.02	0.93
Socioeconomic status (mean ± SD)	12.6 ± 2	12.05 ± 1.6	0.33

Notes: Unless otherwise indicated, data are expressed as mean ± standard deviation (SD) when normally distributed.

Table 2 Clinical, laboratory, radiological, and neurological data of the patients

Clinical data	Data recorded (N = 26)
Systemic manifestations (fever, fatigue, malaise, anorexia, and weight loss)	22 (88%)
Cutaneous	
Malar rash	24 (92.3%)
Photosensitivity	25 (96.2%)
Arthralgia	26 (100%)
Arthritis	23 (88.5%)
Renal	17 (65.4%)
Gastrointestinal findings	7 (26.9%)
Cardiovascular system findings	9 (34.6%)
Pulmonary findings	3 (11.5%)
Daily Activity Index	17.76 ± 6.35
Neuropsychiatric manifestation	
• Anxiety	17 (65.4%)
• Depression	15 (57.7%)
• Headache	10 (38.5%)
• Peripheral neuropathy	7 (26.9%)
• Isolated seizures	6 (23.1%)
• Radiculopathy	5 (19.2%)
• Psychosis	4 (15.4%)
• Dementia	4 (15.4%)
• Myositis	3 (11.5%)
• Stroke	2 (7.7%)
ANA (+ve)	24 (92.3%)
Anti-dsDNA antibody (+ve)	21 (80.8%)
Significant proteinuria (>0.5 g/d or 3+) or cellular casts	20 (76.9%)
Hematologic disorder	
• Anemia	26 (100%)
• Thrombocytopenia	3 (11.5%)
• Leucopenia	9 (34.6%)
ESR	20 (76.9%)
Abnormal MRI of the brain	0 (0%)

Notes: Data are expressed as number (percent).
Abbreviations: ANA, antinuclear antibody; anti-dsDNA, anti-double-stranded DNA; ESR, erythrocyte sedimentation rate; MRI, magnetic resonance imaging.

nonsignificant differences between cases and controls with regard to age, sex, number of education years, and socioeconomic status. The most prevalent neuropsychiatric manifestation was anxiety in 17 cases (65.4%), depression in 15 cases (57.7%), headache in 10 cases (38.5%), peripheral neuropathy in 7 cases (26.9%), isolated seizures in 6 cases (23.1%), psychosis in 5 cases (19.2%), dementia in 4 cases (15.4%), radiculopathy in 4 cases (15.4%), myositis in 3 cases (11.5%), and stroke in 2 cases (7.7%).

Electrophysiological and EEG data are summarized in Tables 3 and 4. There was a significant difference between amplitude of motor NCS of the ulnar nerve of SLE patients and the control group, which means an increased incidence of ulnar axonal neuropathy in SLE patients. Abnormal EEG findings such as high-voltage slow waves and spike slow waves and sharp waves were observed in 19 cases (73.1%) of SLE but in only 6 cases (23.1%) in the control group.

Table 5 illustrates the significant decline in most studied cognitive function tests among the SLE group compared with the control group. In addition, there were higher results in the Hamilton Depression Scale and Hamilton Anxiety Scale.

Table 3 Motor conduction studies of peripheral nerves in cases compared with the control groups

Item	Control N = 26	Cases N = 26	*P* value
Distal latency (ms)			
• Median	3.4 ± 0.245	3.3 ± 0.48	NS
• Ulnar	2.32 ± 0.3	2.56 ± 0.55	NS
• Common peroneal	3.75 ± 0.55	3.98 ± 0.62	NS
Amplitude (MV)			
• Median	12.32 ± 2.96	9.86 ± 5.6	NS
• Ulnar	11.08 ± 1.94	7.56 ± 2.91	0.000
• Common peroneal	4.41 ± 1.33	4.01 ± 4.37	NS
Motor nerve conduction (ms)			
• Median	65.25 ± 6.38	62.58 ± 10.19	NS
• Ulnar	64.61 ± 7.44	62.36 ± 8.4	NS
• Common peroneal	51.72 ± 4.29	51.02 ± 7.7	NS
F-wave latency (ms)			
• Median	24.54 ± 1.16	25.08 ± 4.38	NS
• Ulnar	24.17 ± 1.4	24.07 ± 2.13	NS
• Common peroneal	27.52 ± 2.84	28.27 ± 3.36	NS
H-reflex of tibial (ms)	27.36 ± 4.15	28.38 ± 1.03	NS

Notes: Unless otherwise indicated, data are expressed as mean ± standard deviation when normally distributed.
Abbreviations: MV, mean velocity; NS, nonsignificant.

Table 4 Electroencephalograph (EEG) in cases compared with the control group

Item	Control N = 26	Cases N = 26	Chi-square *P* value
Normal EEG	20 (76.9%)	7 (26.9%)	0.000
Abnormal EEG			
• Focal sharp or slow wave	6 (23.1%)	19 (73.1%)	0.003
• Focal slowing	2 (7.7%)	8 (30.8%)	
• Diffuse slowing	4 (15.4%)	5 (19.2%)	
	0	5 (19.2%)	
Side of focal changes			
• Generalized	6 (23.1%)	13 (50%)	0.005
• On one hemisphere with secondary generalization	0	5 (19.2%)	
• Changes appeared			
◦ Without provocation	2 (7.7%)	9 (34.6%)	0.003
◦ With provocation	4 (15.4%)	9 (34.6%)	
• Repetition			
◦ <5	6 (23.1%)	7 (26.9%)	0.000
◦ >5–10	0	5 (19.2%)	
◦ >10	0	7 (26.9%)	

Notes: Data are expressed as number and percentage.

Table 5 Cognitive function, depression, and anxiety in patients compared with control

Item	Control N = 26	SLE N = 26	*P* value
MMSE score	28.15 ± 1.9	25.81 ± 4.74	0.025
CASI			
Long-term memory	9.5 ± 1.0	8.04 ± 2.12	0.002
Short-term memory	9.9 ± 1.8	7.37 ± 2.94	0.000
Attention	8.1 ± 0.74	7.23 ± 0.86	0.000
Mental manipulation/ concentration	8.3 ± 2.1	6.00 ± 3.08	0.002
Orientation	16.2 ± 3.3	15.88 ± 2.76	NS
Drawing	8.1 ± 2.8	7.96 ± 2.94	NS
Abstract thinking and judgment	8.8 ± 2.9	7.31 ± 2.81	NS
Fluency 4-legged animals	9.7 ± 0.6	8.19 ± 2.83	0.009
Language	7.8 ± 2.0	7.47 ± 1.74	NS
CASI total score	86.6 ± 9.6	74.49 ± 17.33	0.003
Hamilton Depression Scale	6.0 ± 0.6	16.31 ± 8.45	0.000
Hamilton Anxiety Scale	7.5 ± 8.3 (1.607)	20.00 ± 9.37	0.000

Notes: Unless otherwise indicated, data are expressed as mean ± standard deviation when normally distributed.
Abbreviations: CASI, Cognitive Abilities Screening Instruments; MMSE, Modified Mini-mental State Examination; NS, nonsignificant; SLE, systemic lupus erythematosus.

There was a significant increased MV and decreased PI of most studied intracranial vessels in both patient groups compared with the control group. There was a significant increased MV of ACA and VA and nonsignificant decreased PI of most studied intracranial vessels in the patient group compared with the control group (Table 6).

To examine the relationship between SLEDAI cognitive function subscales, laboratory findings, and TCD studies of all patient groups (Table 7), a series of Pearson correlation coefficients was calculated. There were significant negative correlations between SLEDAI and short-term memory, CASI drawing and fluency, and MCA and PCA PI.

Table 6 Intracranial vessels affection in patients and control

Item		Control N = 26	SLE N = 26	PI
MCA	MV (cm/s)	53.04 ± 9.24	58.94 ± 11.85	NS
	PI	0.66 ± 0.1	0.71 ± 0.18	NS
ACA	MV (cm/s)	41.15 ± 24.92	52.39 ± 11.04	0.0141
	PI	0.67 ± 0.13	0.64 ± 0.14	NS
PCA	MV (cm/s)	48.81 ± 11.26	50.45 ± 11.06	NS
	PI	0.61 ± 0.15	0.63 ± 0.12	NS
VA	MV (cm/s)	34.54 ± 17.61	45.47 ± 6.67	0.006
	PI	0.58 ± 0.08	0.58 ± 0.13	NS
BA	MV (cm/s)	42.88 ± 5.05	44.64 ± 21.10	NS
	PI	0.63 ± 0.09	0.61 ± 0.11	NS

Notes: Data are expressed as mean ± standard deviation.
Abbreviations: ACA, anterior cerebral artery; BA, basilar artery; MCA, middle cerebral artery; MV, mean velocity (cm/s); NS, nonsignificant (the mean difference is significant at the 0.05 level [equal variances not assumed]); PCA, posterior cerebral artery; PI, Pulsatility Index; SLE, systemic lupus erythematosus; VA, vertebral artery.

Table 7 Pearson correlation between systemic lupus erythematosus disease activity index and cognitive function subscales, laboratory findings, TCD studies

		R value	*P* value
CASI	Short-term memory	–0.434	0.030[a]
	CASI drawing	–0.479	0.013[a]
	CASI fluency	–0.429	0.029[a]
Laboratory	ANA	0.522	0.006[b]
TCD	MCA PI	–0.414	0.035[a]
	PCA PI	–0.449	0.021[a]

Notes: [a]Correlation is significant at the 0.05 level (2-tailed); [b]Correlation is significant at the 0.01 level (2-tailed); Only significant data are expressed.
Abbreviations: ANA, antinuclear antibody; CASI, Cognitive Abilities Screening Instruments; MCA, middle cerebral artery; PCA, posterior cerebral artery; PI, Pulsatility Index; TCD, transcranial duplex.

Discussion

Neurophysiological and psychometric studies may help to characterize the potential meaning of subclinical neurological involvement. Moreover, they may favor more accurate diagnosis and may provide clinicopathological information regarding its nature.[23] In this study, neurophysiological studies helped in the diagnosis of neurological abnormalities in clinically silent neurological or psychiatric disorders in patients with SLE. The most common type of neuropsychiatric abnormalities recorded in this study was anxiety, followed by depression, headache, peripheral neuropathy, seizures, psychosis, dementia, radiculopathy, myositis, and stroke.

Among NCS, the amplitude of MCV of the ulnar nerve is significantly reduced among SLE patients compared with the control group. These changes indicated predominant axonal neuropathy rather than demyelinating neuropathy among SLE patients. That can be explained by vascular changes rather than other pathological causes of neuropathy, although the pattern of MCV does not permit such a differentiation without a nerve biopsy. This was in agreement with results obtained by Khedr et al in 2001.[24] They noted a significant reduction in amplitude of motor NCS of ulnar, median, and common peroneal nerves among SLE patients compared with the control group. Also, our results were in agreement with Hanly,[25] who reported that sensorimotor neuropathy had been found in up to 28% of SLE patients and frequently occur independently of other disease characteristics.[8]

Abnormal EEG findings were observed in 19 cases (73.1%) but in only 6 cases (23.1%) in the control group. That result was in agreement with Khedr et al in 2001[24] in

which abnormal EEG findings were observed in 73% of cases. In the present study, the most common abnormality was diffuse slow activity, which is generally considered a sign of organic brain disease and is the most common EEG abnormality recorded for SLE.[24] This is matched with previous studies that reported EEG abnormalities among SLE patients.[24,27] In addition, there are significant differences between lupus patients and controls with regard to most studied EEG findings.

Among the many neurological involvements of SLE, cognitive impairment is becoming increasingly recognized.[24] Cognitive function is significant impairment in patients with SLE in comparison with controls in the present study, mainly in short- and long-term memories, attention, mental manipulation/concentration, fluency, and total scores of MMSE and CASI scales. There is no specific or unique pattern of cognitive impairment in SLE, and many individual patients have subclinical deficits. For example, a review of 14 cross-sectional studies of cognitive function in SLE revealed subclinical cognitive impairment in 11%–54% of patients.[25] Fisk et al[28] reported that two patterns of memory dysfunction had been identified in SLE patients. Impaired remote memory appears to be associated with a history of past central nervous system (CNS) involvement (suggesting the presence of a residual neurological deficit), whereas impaired immediate memory and concentration implies increased disease activity that may represent transient and diffuse CNS effects.[28] These deficits are not specific to one brain region or one neuropsychological process, and may reflect both multifocal and diffuse brain diseases. Monastero et al[29] proposed that a frontal temporoparietal dysfunction might account for the cognitive deficits found in patients with SLE. Positron emission tomography (PET)/single photon emission computed tomography (SPECT) studies[30] revealed a hypoperfusion in the frontal, temporal, and parietal lobes mainly in SLE patients.

However, we cannot be completely sure that these cognitive changes are due to the lupus itself or possibly to a manifestation of chronic disease not specific to SLE or neurospsychiatric SLE. A recent paper by Hanly et al[31] demonstrated that there was essentially no difference between SLE, rheumatoid arthritis, and multiple sclerosis patients in cognitive function.

There were significantly higher scores for Hamilton Depression Scale and Hamilton Anxiety Scale in patients with SLE than in the control group, which matches the study by Nery et al.[32] Thirty-five cases out of 71 (49.2%) presented with major depression, and 37 cases (52.1%) presented with anxiety disorders. Several factors might explain these high prevalence rates and include the stress of having a chronic disease and the high doses of corticosteroids commonly used in its treatment.[33] On the other hand, there is intriguing evidence suggesting that some patients with SLE may have organic forms of depression caused by autoimmune lesions in the CNS. For instance, the antiribosomal P antibody is highly associated with both lupus psychosis and severe depression.[33] Furthermore, neuropsychiatric disorders due to SLE activity, such as seizures, strokes, aseptic meningitis, delirium, and psychosis, may also be associated with concomitant depressive symptoms.[33] Nery et al[32] hypothesized that the high prevalence of some anxiety disorders could be linked to feelings of embarrassment experienced in public by some SLE patients due to the skin and facial disfigurements that can result from the disease or treatment. Although a magnetic resonance imaging scan of the brain in all cases was normal, there was early detection of cerebrovascular affection using TCD findings in this study. The middle cerebral artery stem is relatively easy to study. Ultrasound has a sensitivity and specificity of 90%–99% for finding a stenosis or an occlusion. For the more difficult to image intracranial segment of the vertebral arteries and the BA, ultrasound has a sensitivity of 70%–80% and a specificity of 90%–99%.[34]

There are significant increased mean velocities and decreased PI of most studied intracranial vessels. In previous studies, most pathologic conditions affecting the large intracranial arteries result in narrowing, constriction, stenosis, or occlusion of the vessel, which results in increased mean flow velocity and decreased PI.[13,35] These results were matched with a study[35] of 167 patients with SLE evaluated by the TCD technique. Results could not be obtained for 14 patients due to technical difficulties. In the remaining 153 patients, results of 138 TCD techniques were normal, and 15 patients (9%) had one or more abnormalities.[36]

Our results are consistent with the recent article by Gasparovic et al,[37] which demonstrated increased cerebral blood flow and cerebral blood volume that could be consistent with increased mean velocities and decreased PI. This basically demonstrated that neurospsychiatric SLE is often associated with hyperperfusion and that the areas of decreased perfusion observed by PET or SPECT may actually be normal perfusion in certain situations and misinterpreted as areas of reduced perfusion. Our results are consistent with this interpretation. Increased mean velocities and decreased PI could be due to cerebrovasodilation and increased cerebral blood flow.[37]

In this study, abnormalities on TCD (PI) were significantly correlated with clinical disease activity as measured by SLEDAI in the form of MCA ($P = 0.035$ and PCA ($P = 0.021$). These results agree with those of the study by Kron et al.[36] These abnormal findings in TCD in this study can be attributed to the development of vascular changes in SLE, which lead to narrowing and stenosis of cerebral blood vessels.

SLEDAI is a reliable and valid instrument for measuring the clinical state in patients with SLE.[37] In this study, significant negative Pearson correlations were found between SLEDAI, MCA PI, PCA PI, and some cognitive function tests such as short-term memory, drawing, and fluency. In addition, significant positive correlation was found between SLEDAI and ANA laboratory findings. The study of SLEDAI and its correlations is important. With most human attributes, SLE disease activity cannot be measured directly. What is being measured is the observed phenomenon that indicates the existence of this attribute. Assessment of SLE disease activity is challenging due to the multisystem nature of this disease with its diverse range of possible manifestations, as any part of the body can be affected. Furthermore, involvement of a system could lead to various manifestations, adding to its complexity.[38,39] Moreover, we can explain these significant correlations as an increase in severity of the disease with more deterioration in cognitive function.

Disclosure

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