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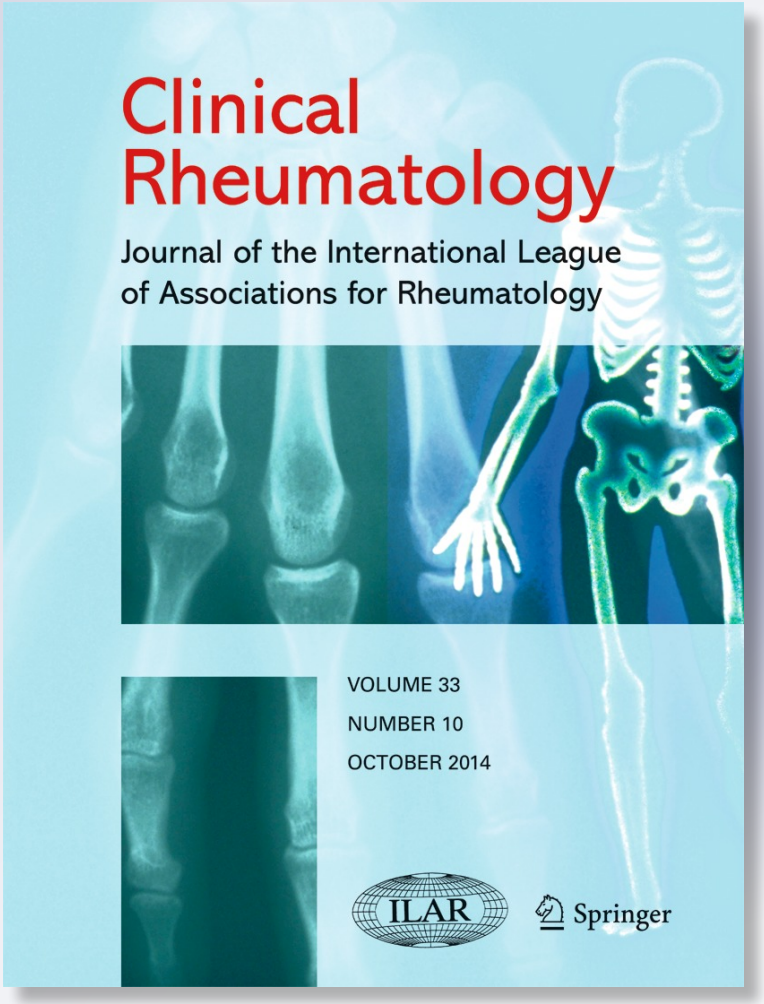
Clinical Rheumatology
Journal of the International League of Associations for Rheumatology

ISSN 0770-3198
Volume 33
Number 10

Clin Rheumatol (2014) 33:1459-1466
DOI 10.1007/s10067-014-2679-y



Springer

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ORIGINAL ARTICLE

Detection of asymptomatic cranial neuropathies in patients with systemic lupus erythematosus and their relation to antiribosomal P antibody levels and disease activity

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Received: 13 January 2014 / Revised: 27 April 2014 / Accepted: 27 April 2014 / Published online: 24 May 2014

Abstract The objectives of this study are to assess the risk of asymptomatic cranial neuropathy among patients with systemic lupus erythematosus (SLE) and find any association with disease activity and antiribosomal P antibodies. This study is a case-control study including 60 female patients and 30 healthy female controls. Disease activity was measured with the SLE disease activity index (SLEDAI). All patients were evaluated using evoked potentials, blink reflex, and levels of antiribosomal P antibodies. Patients with abnormal electrophysiological parameters had significantly higher levels of antiribosomal P antibodies (P=0.034) and secondary antiphospholipid syndrome (P=0.044). Antiribosomal P antibodies (odds ratio 5.4, 95 % confidence interval 1.002–1.03, P=0.002) and presence of anti-DNA antibodies (odds ratio 1.01, 95 % confidence interval 1.2–24.8, P=0.032) were independent risk factors for the presence of the abnormal electrophysiological parameters. Disease duration was positively correlated with wave 1 of the auditory brain reflex (P<0.001) and a latency of the evoked blink reflex (component R1, P=0.013). SLEDAI scores were positively correlated with latencies of the visually evoked potential (P100, P=0.02), wave 1 of the auditory brain reflex (P<0.001), and a latency of the evoked blink reflex (R2c, P=0.005). Steroid dosage was negatively correlated with P100 latencies (P=0.042) and components of the evoked blink reflex (R1, P=0.042; R2i, P=0.041; R2c, P<0.001). Because abnormalities in the visually evoked potential and blink reflex were associated with antiribosomal P antibodies, they can be useful for detecting asymptomatic cranial neuropathy. Further studies on large number of patients should be done to determine any association.

Keywords Antiribosomal P antibodies · Auditory brain reflex · Evoked blink reflex · Systemic lupus erythematosus · Visually evoked potential

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Introduction

Systemic lupus erythematosus (SLE) is a chronic multisystem autoimmune disease of unknown etiology that most commonly affects the skin and the musculoskeletal system. Neurologic manifestations are well recognized with a variety of focal and diffuse neuropsychiatric symptoms preceding or following diagnosis [1]. Cranial neuropathies in SLE have been reported to occur in 5–42 % of cases with neurologic manifestations [2], the most common being retinopathy secondary to vasculitis [3]. Many of these SLE symptoms in the central nervous system (CNS) derive from ischemia, which is most commonly caused by antiphospholipid antibodies or accelerated atherosclerosis and much less commonly caused by CNS vasculitis [4]. Another subset of CNS problems results from antibodies that reversibly alter neuronal functions. Among these antibodies, those related to ribosomal P probably play a role in lupus-induced psychosis [5]. These autoantibodies are directed against three highly conserved phosphorylated P proteins

[6]. Autoantibodies recognizing the ribosomal P protein, first characterized in 1985 [7], are highly specific for SLE [8, 9] and are associated with disease activity and neuropsychiatric events [10]. High levels of antiribosomal P antibodies have been found in psychotic SLE patients [11] and in those with depressive/psychotic SLE [12]. Autoimmune sensory neural hearing loss is a rare disease of unknown etiology that was first described by McCabe in 1979 [13]. Its pathogenesis is still unclear, and its prognosis is often poor. Different mechanisms for it have been proposed, such as vasculitis secondary to SLE, microinfarctions of the capillaries or arterioles in the temporal bone, and thrombosis in the otologic region (in patients with SLE and those with antiphospholipid syndrome) [14]. Our goal was to assess the risk of asymptomatic cranial neuropathies among SLE patients and their relation to antiribosomal P antibody levels and disease activity.

Patients and methods

Study design

The study was conducted as a case-control study to assess the risk of asymptomatic cranial neuropathy among SLE patients. All subjects were recruited from the rheumatology departments from the hospitals at Cairo University and Fayoum University. All participants were informed about the aim of the study and provided their written informed consent in accordance with the ethical principles for human investigations, as outlined in the 2nd Helsinki Declaration. The allocation of the Ethics Committee was made by the department secretary, who had no other role in the study. A letter informing them of the study was sent to the primary-care physician of each patient.

Patients

Study population

Sixty female Egyptian SLE patients who fulfilled the 1982 revised criteria of the American Rheumatism Association for the classification of SLE [15] participated in the study (mean age 30.5±9.6 years). Thirty age- and sex-matched healthy controls (mean age 30.4±7.1 years) with no history of autoimmune or other rheumatic diseases also participated. Full medical histories were obtained from all SLE patients. These included a general examination followed by cardiopulmonary, abdominal, neurological, and locomotor-systems examinations. Blood pressure was measured on multiple occasions. Systemic hypertension was recorded when systolic blood pressure was ≥140 mmHg, diastolic blood pressure was ≥90 mmHg, or when antihypertensive medication was taken. No patient was diabetic or had a history of infectious disease, vitamin deficiencies, or multiple sclerosis. Antiphospholipid syndrome was diagnosed according to the Sapporo criteria [16], based on evidence of a stroke with a documented neurologic deficit, evidence of a vascular thrombotic event outside the CNS, or a typical obstetric history with the presence of antiphospholipid antibodies (anticardiolipin IgG, anticardiolipin IgM, or lupus anticoagulant) on at least two occasions, 6 weeks apart. Assessment of disease activity was performed using the systemic lupus erythematosus disease activity index (SLEDAI) [17].

Routine laboratory investigations including complete blood count, liver and kidney functions via the Jaffe kinetic method, urine analysis and 24-hours urine samples were collected to estimate total urinary protein levels via the colorimetric method. Blood and urine samples were always collected on the same day. Immunological assays for antinuclear antibodies and antideoxyribonucleic acid antibodies were conducted by indirect immunofluorescence, and those for serum C3 and C4 levels by nephelometry (Beckman, USA). Detection of the anticardiolipin antibodies was performed using the enzyme-linked immunosorbent assay, detection of lupus anticoagulant was conducted using the dilute Russell viper venom time clotting assay, and detection of antiribosomal P antigen was determined by Western blotting of purified ribosomes [18]. Brain images of each patient were obtained using magnetic resonance imaging (MRI). MRI was performed using a Diasonics MT/S system employing a super-conducting 0.5 tesla (T) magnet operating at 0.35 T. All images were obtained with multislice, spin-echo technique imaging hydrogen nuclei; 7-mm-thick sections at 10-mm intervals were obtained at a 1.7×1.7-mm resolution. Cranial nerve (II, V, VII, and VIII) function was assessed by examination of evoked potentials and the blink reflex, which was carried out at the Clinical Neurophysiology unit at Kasr El Aini Hospital using a Nihon Kohden® Neuropack machine (MEB_9200K, Japan). The patients were classified into two groups: group 1 had abnormal electrophysiological parameters and group 2 did not. Electrophysiological parameters of the cranial nerves were correlated with clinical and laboratory parameters, disease activity measure (SLEDAI), and steroid intake, and findings were compared across the two patient groups.

The control subjects were unrelated to patients but were ethnically and socioeconomically similar. Physical examinations for them were normal, with blood pressure <135/85 mmHg, no urine abnormalities, and no history of autoimmune or rheumatic disease or any other diseases with a known genetic or hereditary predisposition.

The electrical blink reflex

Silver chloride disc surface electrodes were placed bilaterally on the orbicularis oculi muscles below the outer canthi. The reference electrode was placed on the lateral canthus, and the

ground electrode was placed on the forehead. The impedance was kept below 5 kΩ. The sweep speed was set at 100 ms, and the band pass filter was 1–2,500 Hz. Square-wave electrical pulses were randomly delivered to the supraorbital nerves at an inter-stimulus interval of at least 30 s (to avoid habituation) with a pulse duration of 0.2 ms. The intensity of the stimulus was gradually increased until the threshold provoking a response was found. This was followed by a gradual reduction in stimulation intensity until the response vanished. This procedure was repeated twice to define the minimum intensity that provoked a blink response. The intensity of stimulation was then adjusted to the value that provoked the maximum response amplitude. Four trials were carried out to ensure reliability and reproducibility. The electrical blink reflex (EBR) was used to test the trigeminal and facial nerves. R1 is mediated by a disynaptic connection between the main sensory nucleus and the ipsilateral facial motor nucleus, and R2 responses are mediated by a multisynaptic pathway between the nucleus of the spinal tract of cranial nerve V and both ipsilateral and contralateral facial nuclei. The efferent pathway for both R1 and R2 is mediated by the projection of the facial nerve to the orbicularis oculi muscles [19].

Visually evoked potentials

A recording electrode was placed 5 cm above the inion, and the reference electrode was placed over the forehead (Fz), according to the 10-20 international system. The ground electrode was placed on the ear tragus. The visual stimulus was an alternating checkerboard pattern. We stimulated each eye separately at 1 Hz with a checkerboard pattern sized to 32° of visual angle. The patient was seated at a distance of 1 m from the pattern stimulator and asked to fixate on a small spot placed in the center of the monitor. Evoked potentials were recorded from 100 trials, summed, and averaged. Optic-nerve function was assessed using the latency of the P100 visually evoked potential (VEP); the P100 is a positive evoked potential that occurs approximately 100 ms after visual stimulation. Normal P100 latencies range between 94 and 114 ms, and normal P100 amplitudes range between 2.5 and 31 μv [20]. Responses were thus considered abnormal if P100 was absent or either if its latency exceeded 115 ms after stimulation through at least one eye or if the amplitude difference between eyes was greater than 50 %.

Brain stem auditory evoked potentials

A recording electrode was placed on the ipsilateral earlobe, and the reference electrode was placed on the vertex (Cz), according to the 10-20 international system. The ground electrode was placed over the forehead. Monaural auditory stimuli consisted of a clicking sound delivered at 10 kHz. Square-wave pulses were delivered through earphones at a rate of 11 clicks/s. The intensity of the click was adjusted to be 60 db above the hearing threshold. Masking noise was applied to the unstimulated ear 30 db below the click intensity. Stimuli were presented 2,000 times, and average latencies were calculated for analysis [20].

Data analysis

The data were coded and entered using the statistical package SPSS version 15. The data were summarized with descriptive statistics: the mean, standard deviation, median, minimum, and maximum values as quantitative variables and number and percentage as qualitative values. Statistical differences between groups were tested using the chi-square test for qualitative variables, two-sample Student's *T* test for normally distributed qualitative variables, Mann-Whitney *U* test for nonparametric variables, and the Kruskal-Wallis test for quantitative variables that were not normally distributed. Pearson correlation was used for detection of the relation between two variables. Binary logistic regression analysis was conducted to estimate the association between abnormal electrophysiological parameters and the estimated risk factors. *P* values less than 0.05 were considered statistically significant [21].

Results

Characteristics of the patients

Sixty female SLE patients and 30 healthy female subjects participated in this study. The demographics, clinical features, and laboratory parameters for all subjects are presented in Table 1. Evidence of vasculopathy in the form of Raynaud's phenomenon and cutaneous vasculitis (palpable purpura, papules, and plaques) was found in 30 SLE patients (50 %). All SLE patients were positive for antinuclear antibodies, 42 had hematological abnormalities, with anemia being present in 40 of them (67 %), 20 had leucopenia (33 %), and 16 had thrombocytopenia (26 %). Thirty-three patients had nephropathy, which was defined as persistent 24-h proteinuria >0.5 g, active sediment (dysmorphic urinary blood cells, granular casts), or serum creatinine >1.2 mg/dl or evidence of lupus nephritis on a renal biopsy. No patients had clinical cranial nerve affection, but ten patients (16.6 %) had psychosis and three had seizures (5 %). Eighteen (30 %) had secondary antiphospholipid syndrome. Five patients had a history of stroke, and four had a history of transient ischemic attacks. Twelve patients had recurrent pregnancy loss, two had superficial venous thrombosis, and six had deep venous thrombosis. All patients were taking steroids (15–50 mg/day), 45 were taking hydroxychloroquine (200–400 mg/day), 25 were taking azathioprine (100–150 mg/ day), and 30 were receiving

Table 1 Demographic, clinical, and laboratory data from the SLE patients

Parameter	SLE patients (*N*=60)
Age (years), mean ± SD	30.5±9.6
Disease duration (years), mean ± SD	3.6±4.3
ESR (mm/1st hour), mean ± SD	71.6±39.2
Hemoglobin (g/dl), mean ± SD	12.4±1.9
WBCs (10^3/mm^3), mean ± SD	7.2±3.8
Platelets (10^3/mm^3), mean ± SD	223±78.8
Serum creatinine (mg/dl), mean ± SD	1.8±0.3
Serum albumin (gm/dl), mean ± SD	3.3±0.8
Urine protein (gm/24 h), mean ± SD	1.2±0.9
FBS (mg/dl), mean ± SD	94.2±14.8
SLEDAI, mean ± SD	20.1±6.4
Seropositive ANA count (percent)	60 (100 %)
Anti-dsDNA count (percent)	51 (85 %)
Antiribosomal P (pg/ml), mean ± SD	30.1±71.9
Fever count (percent)	20 (33 %)
Malar rash count (percent)	30 (50 %)
Photosensitivity count (percent)	35 (58 %)
Alopecia count (percent)	5 (8 %)
Oral ulcers count (percent)	30 (50 %)
Vasculopathy count (percent)	20 (33 %)
Hypertension count (percent)	7 (12 %)
Arthritis count (percent)	51 (85 %)
Nephritis count (percent)	33 (55 %)
Serositis count (percent)	39 (65 %)
Secondary APS count (percent)	18 (30 %)
Brain MRI changes count (percent)	6 (10 %)

ESR erythrocyte sedimentation rate, *WBCs* white blood cells, *FBS* fasting blood sugar, *SLEDAI* systemic lupus erythematosus disease activity index, *ANA* antinuclear antibodies, *Anti-dsDNA* antidouble-stranded DNA antibodies, *ACL* anticardiolipin, *APS* antiphospholipid syndrome, *MRI* magnetic resonance imaging

monthly cyclophosphamide pulse therapy depending on the extent of renal lesion (700–1,000 mg).

Brain MRI and electrophysiological parameters

Brain MRI revealed CNS differences in six patients (10 %) that presented as small hyperintense foci in the T2-weighted images as shown in Fig. 1. The MRIs for SLE patients with abnormal electrophysiological parameters did not significantly differ from those without abnormal electrophysiological parameters. Analysis of the electrophysiological parameters showed that cranial nerve VIII was the most commonly affected cranial nerve (20 %), followed by cranial nerve VII (15 %), cranial nerve II (10 %), and cranial nerve V (5 %). Twenty-four SLE patients (40 %) appeared to show abnormal electrophysiological parameters in the form of a delayed

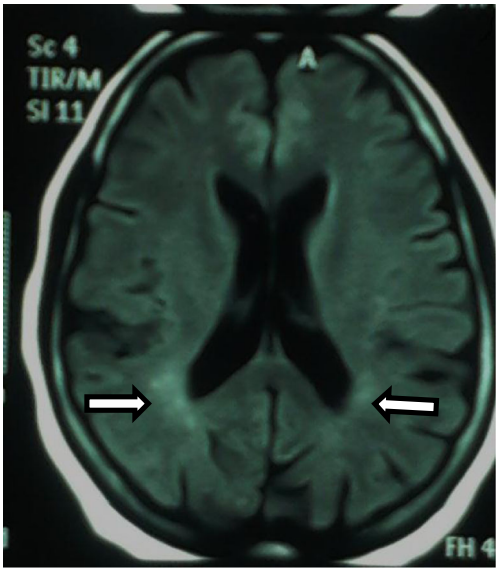

Fig. 1 Brain MRI vasculitis in the form of small tiny hyperintense foci in T2-weighted images

latency (41 ms) in the R2i component of the EBR after stimulating the right supraorbital nerve and bilaterally delayed P100 after visual stimulation. P100 amplitudes were not abnormal in SLE patients. Average P100 latencies over the right (130.8 ms) and left (126.3 ms) hemispheres are shown in Fig. 2, along with P100 amplitudes.

Here, we found that SLE patients with abnormal electrophysiological parameters had higher levels of antiribosomal P antibodies and secondary antiphospholipid syndrome than SLE patients with normal electrophysiological parameters (P=0.034, P=0.044, respectively) (Table 2). As shown in Table 3, antiribosomal P antibodies were significantly and positively correlated with P100 latencies, ABR waves 3 and 5 over the left hemisphere (wave 3 is generated by the superior olivary complex, and wave 5 is generated by the inferior colliculus), and with the latencies of the R1, R2i, and R2c components of the EBR over the right hemisphere. In addition, we found that disease duration significantly and positively correlated with latency of ABR-wave 1 over the right hemisphere (generated by the cranial nerve VIII) and with latency of the R1 of component of the EBR over the left hemisphere (P<0.001 and 0.01, respectively). SLEDAI score was significantly and positively correlated with P100 latency, latency of ABR-wave 1 over the right hemisphere, and R2c latency over the right hemisphere. Furthermore, steroid dose was significantly and negatively correlated with left P100 and right R1, R2i, and R2c (P=0.042, P=0.042, P=0.041, and P<0.001, respectively).the asterisk reflects the significant difference where p <0.005

Our study also found that antiribosomal P antibodies (odds ratio [OR] 5.4, 95 % confidence interval [CI] 1.002–1.03, P= 0.002) and the presence of anti-dsDNA antibodies (OR 1.01, 95 % CI 1.2–24.8, P=0.032) were independent risk factors for the presence of the abnormal electrophysiological parameters.

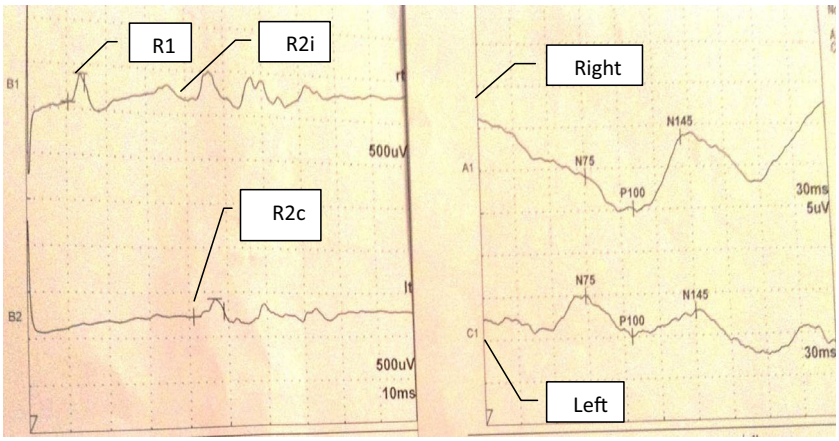

Fig. 2 The *left trace* shows a normal R1 latency=10.4 ms, delayed latency of R2i (41 ms), and a normal R2c (41.1 ms) on stimulating the right supraorbital nerve. The *right trace* shows T.V. pattern reversal visual evoked potential studies of the same patient showing delayed absolute latency of P100 responses bilaterally. P100 latency over the *right side*=130.8 ms, and that of the *left side*=126.3 msec (*A1* right, *C1* left). With normal P100 amplitude bilaterally, that of the *right side*=4 uv and of the *left side*=5 uv. *R1* response 1, *R2i* response 2 ipsilateral, *R2c* response 2 contralateral

Table 2 Comparison between patients with normal and abnormal electrophysiological parameters (EPs)

	Abnormal EP study group (*N*=24)	Normal EP study group (*N*=36)	Odds ratio	95 % CI	*P* value
Disease duration (mean±SD)	4.4±4.6	3.1±3.9		−3.6–0.9	0.212
Age (mean±SD)	30.9±11.9	30.3±7.9		−6.2–4.9	0.845
ESR (mean±SD)	67.3±35.8	74.5±41.6		(−13.5)–28.03	0.522
HGB (mean±SD)	10.8±2.3	10.1±1.5		(−1.8)–0.4	0.234
WBCs (mean±SD)	8.1±4	6.5±3.5		(−3.6)–0.3	0.123
Platelets (mean±SD)	250.9±71.7	204.4±78.8		(−86.6)–(−6.3)	0.022
Serum albumin (mean±SD)	3.3±0.9	3.4±0.6		(−0.3)–0.5	0.644
Steroid dose (mean±SD)	24.4±15.6	28.3±13.1		(−3.5)–11.4	0.313
HQN dose (mean±SD)	300±176.9	300±175.7		(−92.9–92.9	1.242
Azathioprine dose (mean±SD)	62.5±55.7	62.5±55.3		(−29.2)–29.2	1.436
CYC dose (mean±SD)	0.9±1.6	0.4±0.9		(−1.2)–0.3	0.223
SLEDAI					
Moderate	9	18			0.823
Severe	15	9			
Very severe	0	9			
Psychosis	7	3	1.6	0.3–8.5	0.712
Seizures	3	0	1.1	0.9–1.3	0.064
Nephritis	12	21	0.7	0.3–2	0.521
Serositis	18	21	2.1	0.7–6.7	0.246
2ry APS	12	6	1.7	1.5–16.3	0.044
Arthritis	21	30	1.4	0.3–6.2	0.723
Myositis	6	9	1.1	0.3–3.3	1.245
Vasculitis	3	3	0.2	0.03–0.6	0.734
Positive antiribosomal P a.b.	9	6	3.2	1.3–10.1	0.034
Low complement	9	12	1.2	0.4–3.5	0.723
Anti-dsDNA a.b.	18	33	0.3	0.06–1.2	0.081
CRP	9	21	0.4	0.1–1.2	0.112
Brain MRI changes	3	3	1.6	0.3–8.5	0.725

SLEDAI systemic lupus erythematosus disease activity index, *SLICC* Systemic Lupus International Collaborating Clinics, *2ry AP* secondary antiphospholipid syndrome, *ESR* erythrocyte sedimentation rate, *WBCs* white blood cells, *HGB* hemoglobin, *Anti-dsDNA* antidouble-stranded DNA antibodies, *CRP* C-reactive protein, *HQN* hydroxychloroquine, *CYC* cyclophosphamide

Table 3 Correlations between electrophysiological findings and clinical and laboratory parameters

Electrophysiological parameters		Disease duration	SLEDAI	Antiribosomal P antibody	Steroid dose
Right VEP P100 latency	*P* value	0.072	0.021*	0.008*	0.081
	r	0.233	0.294	0.341	−0.232
Left VEP P100 latency	*P* value	0.130	0.033*	0.011*	0.042*
	r	0.192	0.282	0.314	−0.262
Right VEP amp	*P* value	0.093	0.382	0.932	0.291
	r	0.223	0.112	−0.010	0.131
Left VEP amp	*P* value	0.771	0.942	0.411	0.043*
	r	0.031	0.011	0.101	0.251
Right ABR latency W1	*P* value	<0.001*	<0.001*	0.613	0.092
	r	0.452	0.472	−0.061	0.221
Right ABR latency W3	*P* value	0.692	0.392	0.213	0.713
	r	0.051	0.112	−0.152	0.051
Right ABR latency W5	*P* value	0.561	0.411	0.762	0.6743
	r	0.072	0.121	−0.043	−0.053
Left ABR latency W1	*P* value	0.063	0.441	0.653	0.113
	r	0.233	0.113	0.062	0.223
Left ABR latency w 3	*P* value	0.821	0.172	0.006*	0.222
	r	0.020	0.174	0.352	−0.162
Left ABR latency W5	*P* value	0.372	0.544	0.008*	0.134
	r	0.112	0.084	0.334	−0.193
Right EBR R1	*P* value	0.531	0.734	0.034*	0.042*
	r	0.094	0.053	0.245	−0.322
Right EBR R2i	*P* value	0.623	0.623	0.033*	0.041*
	r	0.082	0.082	0.323	−0.332
Right EBR R2c	*P* value	0.524	0.005*	0.003*	<0.001*
	r	0.083	0.432	0.432	−0.423
Left EBR R1	*P* value	0.013*	0.443	0.112	0.922
	r	0.324	0.134	−0.212	0.003
Left EBR R2i	*P* value	0.923	0.072	0.112	0.732
	r	0.013	0.223	0.234	−0.06
Left EBR R2c	*P* value	0.734	0.311	0.064	0.312
	r	0.052	0.123	0.232	0.133

* $p < 0.005$

VEP visual evoked potential, *ABR* auditory brain reflex, *W1* wave 1, *W3* wave 3, *W5* wave 5, *EBR* evoked blink reflex, *R1* response 1, *R2i* response 2 ipsilateral, *R2c* response 2 contralateral

In contrast, analysis showed that secondary antiphospholipid syndrome and differences in brain MRI were not risk factors (P=0.421 and P=0.632, respectively).

Mean antiribosomal P antibody levels were significantly different between SLE patients (30.1±71.9 pg/ml) and controls (2.1±1.4 pg/ml; P=0.003). Furthermore, antiribosomal P antibodies were significantly associated with SLE patients (OR 9.7, 95 % CI 2.1–44.5, P=0.001), but not with controls (P=0.821).

Discussion

Neuropsychiatric lupus is a well-recognized complication of systemic lupus erythematosus (SLE) and includes a wide variety of neurological manifestations that occur in 25–70 % of SLE patients. The central or peripheral nervous system may be involved, and the manifestations may be diffuse [22]. Although isolated cranial nerve involvement is rare, it occasionally appears as an initial or predominant sign of neuropsychiatric lupus [23, 24]. Pathological studies have shown that neurological involvement is mainly at the microvascular level, and it is observed in 65 % of cerebral lupus that primarily affects arterioles of a diameter less than 100 μm [25].

A study conducted by Bruns and Meyer [26] provides some theories regarding the presence of asymptomatic cranial neuropathy in SLE patients. They assert that it could be related to (1) autoantibodies related to neuronal antigens, ribosomes, and phospholipids; (2) vascular lesions (vasculitis or antiphospholipid antibody-mediated thrombotic vasculopathy); or (3) inflammation related to local cytokine production.

Early detection of asymptomatic cranial neuropathies in SLE patients can be of great value. While no specific serological or imaging marker has been found, the results of our study show that antiribosomal P antibodies are an independent risk factor for abnormal electrophysiological parameters associated with some SLE patients and that these patients have a significant increase in the production of antiribosomal P antibodies ($P=0.034$). This could be related to the increased prevalence of psychosis in our SLE patients with abnormal electrophysiological responses, which coincides with several studies that report antiribosomal P to be associated with SLE psychosis. These studies suggest that because neurons are rich in ribosomes, the presence of small vessel infarcts in the brains of patients with cerebral lupus and the neuronal degeneration in these lesions may lead to increased antiribosomal P antibody production [8, 11, 27]. In contrast, others have shown no association of antiribosomal P antibodies with cerebral manifestations in SLE patients and did not detect antiribosomal P antibodies in the cerebrospinal fluid [28–30].

We found a significant difference in secondary antiphospholipid syndrome between patients with and without abnormal electrophysiological parameters ($P=0.044$) that could be explained by ischemic cranial neuropathy due to venous thrombosis and multifocal microinfarcts [31]. Our study also showed that among the cranial nerves examined, cranial nerve VIII was the most frequently abnormal nerve in SLE patients, resulting in asymptomatic sensorineural hearing defects that are in agreement with other reports [32, 33].

Similar to other studies showing that about 63 % of the neurological manifestations associated with SLE occur within the first year of diagnosis [34, 35], we found that disease duration was significantly longer in SLE patients with abnormal electrophysiological parameters than in those with normal electrophysiological parameters. In addition, SLEDAI score correlated with increases in P100, ABR-wave 1, and R2c latencies. Further, steroid dose had a significant negative relationship with P100, R1, R2i, and R2c latencies, which agrees with another study showing that cranial neuropathy has been recognized as a feature of nervous-system manifestation in lupus and that treatment with an oral dose of prednisolone (1 mg/kg/day) was useful [36].

In conclusion, asymptomatic cranial neuropathy in SLE patients can be detected via visually evoked potentials and the evoked blink reflex. Presence of antiribosomal P antibodies or secondary antiphospholipid syndrome in SLE patients may be considered a high risk for development of asymptomatic cranial nerve affection. If feasible, evoked potentials may be recorded and analyzed in active SLE patients regardless of the presence of any symptoms, and signs of any cranial nerve affection can be detected at an early stage. To confirm our results, we propose that larger-scale multicenter studies may help to establish the true significance of any association.

Conflict of interest The authors have no conflicts of interest.

Funding This research received no specific grant from any funding agency in the public, commercial, or nonprofit sectors.

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