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Perfusion-weighted MR Imaging in Cerebral Lupus Erythematosus

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Abstract

Rationale and Objective—NPSLE is a diagnostically challenging, severe, and life-threatening condition, which is currently lacking a “gold standard.” Our aim with this study is to look for MR perfusion differences in NPSLE, SLE, and HC patients and correlate our findings with clinical parameters.

Materials and methods—24 NPSLE patients, 21 SLE patients, and 21 HC underwent dynamic susceptibility contrast enhanced MR perfusion using a 3 T scanner. Nine prospectively selected intracranial ROI were placed in white and grey matter and the CBF, CBV, and MTT values were calculated. Subjects underwent clinical evaluation with SLEDAI and serum antibodies.

Results—The SLE patients had higher CBF and CBV compared to the HC overall ($p=0.01$) and in specific areas ($p=0.03$ – 0.048). SLE patients with signs of active disease (elevated SLEDAI and anti-dsDNA) had significantly elevated CBV, CBF, and MTT in the posterior cingulate gyrus ($p=0.01$ – 0.02). No significant difference was seen in the MR perfusion measurements of NPSLE patients compared to SLE and HC, although the NPSLE patients also showed higher CBV variability compared to the SLE ($p=0.0004$) and HC cohort ($p<0.0001$).

Conclusion—SLE patients have increased CBV and CBF compared to healthy controls. The SLE patients with clinical markers for active disease have elevated CBV, CBF, and MTT in the posterior cingulate gyrus. NPSLE patients show increased variability in perfusion measurements, which may explain why susceptibility contrast enhanced MRI has not yet provided a specific target for NPSLE.

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Keywords

SLE; lupus; neuropsychiatric lupus; perfusion; MRI

Introduction

Neuropsychiatric systemic lupus erythematosus (NPSLE) is a severe and life-threatening condition, reported to occur in 25–70% of systemic lupus erythematosus (SLE) patients¹. NPSLE patients present with protean clinical manifestations such as: aseptic meningitis, stroke, TIA, cerebral venous sinus thrombosis, delirium/dementia, demyelinating syndrome, headaches, movement disorders, psychosis, or mood/anxiety disorders^{2,3}.

NPSLE patients have a decreased quality of life and a worse prognosis compared to SLE patients^{4,5,6}. Therefore, it would be clinically and prognostically helpful to develop a “gold standard” to diagnose patients with NPSLE. Although several studies have described abnormal imaging findings and cortical atrophy in NPSLE patients, few studies have looked at dynamic perfusion in lupus patients. In contrast to the previously published studies, we wanted to see if lupus patients had focal areas of perfusion derangement and decided to use frontal white matter as a denominator/constant for our perfusion calculations^{7,9}.

The aim of our study is to use dynamic susceptibility contrast MRI, a MR perfusion technique, to evaluate for differences in NPSLE, SLE, and healthy control (HC) patients in specific brain regions and correlate our findings with clinical/serological markers.

Materials and Methods

Subjects

For this study we included 24 consecutive patients (24 female, age 23.9–70, mean age 44.1 years) with acute NPSLE, defined as one or more neuropsychiatric manifestations within 2 weeks prior to inclusion in the study, 21 consecutive patients (19 female, 2 male, aged 23.6–64.8, mean age 43.4 years) with SLE, without current or past history of neuropsychiatric symptoms, and 21 healthy controls (HC) (19 female, 2 male, aged 21.2–64.9, mean age 43.6 years). The classification of NPSLE was based on the 19 American College of Rheumatology 1997 case definitions¹⁰. In order to participate in the study, individuals needed to fulfil 4 or more of the American College of Rheumatology classification criteria and present within 2 weeks of the initial neuropsychiatric event. All participants were recruited from the Department of Internal Medicine, Division of Rheumatology, and in some case of patients with a previous known diagnosis of SLE or NPSLE from the Department of Emergency Medicine at the University of [...]. All patients had a clinical evaluation by the rheumatologist at time of admission and prior to the MRI examination. Informed consent was obtained for all participants and the study was approved by the local Institutional Review Board. Exclusion criteria included: previous/known drug abuse, alcohol abuse, diabetes, stroke and/or renal insufficiency. Patients with stroke and diabetes were excluded since these diseases are known to affect the cerebral vasculature and therefore the CBF and MTT might be effected¹¹. Three patients in the NPSLE group, 3 in the SLE group and 2 HC were excluded from the analysis due to poor quality/motion artifacts. Twenty-one NPSLE (21 females, mean age 43.7±11.8), 18 SLE patients with no neurological symptoms (17 females, 1 male, mean age 42.7±14.3), and 19 HC (19 females, mean age 44.5±14.3) were included in the final analysis. No significant differences in age, gender, disease duration, or age at diagnosis was found among the groups, as shown in table 1.

MR imaging and MR perfusion

All subjects underwent conventional magnetic resonance imaging (MRI) pre and post contrast administration on a 3T scanner with following sequences: T2-weighted (TR/TE 4800/80 msec; matrix 400×309 ; slice thickness 4; gap 1), fluid-attenuated inversion recovery (TR/TI/TE 11000 msec/ 2800 msec/ 125 msec; matrix 352×170 ; slice thickness 4mm; gap 1) and T1-weighted pre and post contrast (TR/TE 9.8/4.6 msec; matrix 236×200 ; slice thickness 3 mm; no gap). The field of view was 230–240 mm.

MR perfusion was performed as a dynamic susceptibility contrast enhanced MR perfusion sequence by means of echo planar imaging and fast field echo MR (TR/TE 1500/50 msec; matrix 112×109 , slice thickness 4.4 mm, 19 slices, field of view 230×230 mm, flip-angle 40 degrees, number of signal averages 1, parallel imaging acceleration factor 3, dynamic phases 45, acquisition time 2:18 minutes, a single dose of Magnevist per body weight was injected at 2cc/sec followed by a 20cc saline flush).

Imaging post-processing and analysis

Conventional MR images were interpreted by a neuroradiology attending (27 years' experience) that was blinded to patient history and asked to comment on morphological abnormalities such as acute or old infarcts, hemorrhage, focal or diffuse brain atrophy, focal lesions or pathological contrast enhancement and for any additional lesions not related to SLE. Lesion burden in form of white matter T2/FLAIR hyper-intensive lesions was defined as grade 0=none, grade 1=mild (1–5 small white matter lesions), grade 2=moderate (5–10 white matter lesions), or grade 4=severe (>10 white matter lesions). Any clinically relevant findings on structural MRI were reported to the patient's primary physician.

Scans were post-processed using the Philips T2* perfusion tool (Philips Medical Systems, Best, The Netherlands), a medium smoothing kernel, and the right middle cerebral artery was selected for the arterial input function. A total of nine 10–15 mm² specific regions of interest were placed by PW, in a number of normal appearing gray and white matter regions (e.g. areas demonstrating normal appearance on T2 and FLAIR weighted images e.g. areas without any focal white matter lesions): posterior cingulate cortex, right frontal white matter, right occipital white matter, right and left hypothalamus, right and left parahippocampal gyrus, and right and left posterior thalamus [Figure 1]. The locations of these ROIs were chosen *a priori* because of their known involvement in SLE and NPSLE patients or because they had shown abnormalities in previous neuroimaging studies¹². Since the patients overall presented with none or only mild atrophy, no normalization to gray matter atrophy was performed. The CBF, CBV, and MTT values were generated and then divided by the respective CBF, CBV, and MTT measurements from the different ROI's placed in the normal appearing frontal white matter to create the relative rCBF, rCBV, and rMTT values.

Subjects' clinical assessment

All patients and controls were submitted to a standardized clinical and neurological examination including medical history, physical exam, standard laboratory assessment and a Mini Mental State examination¹³. SLE and NPSLE patients underwent required laboratory tests to determine disease activity by the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) [see table 2], anti-dsDNA antibody, and anti-cardiolipin antibody status¹⁴. SLE was considered active with a SLEDAI score > 6. Disease duration was defined as the time between the diagnosis of SLE and the day of the MRI.

Statistical analysis

Continuous variables were expressed as mean $\pm$ standard deviation. Categorical variables were summarized using counts and percentages. MR perfusion findings (relative CBF, CBV and MTT) were compared between the three patient cohorts by two sample t-test or Wilcoxon rank-sum test when appropriate (lack of normality). A Spearman correlation analysis was conducted to assess the relationship between these findings (of the brain areas individually and as a whole) and the clinical parameters. A probability (p) value of 0.05 or smaller was considered significant for all hypothesis tests. The above analyses were performed using SAS 9.2 (SAS Institute Inc.; Cary, NC).

Age, disease duration, SLEDAI, anti-dsDNA was compared using an ANOVA for comparison of all three groups. A two-sample t-test or Wilcoxon rank-sums test (when the normality assumption was not met), was used in case only SLE and NPSLE patients were compared. Fisher's exact test was used to compare gender distribution. A nonparametric Kruskal-Wallis Test was used to look for statistical significant differences among the distributions of white matter lesion burden between the groups ($p=0.0026$). Thereafter a nonparametric Mann-Whitney Test was used to assess the differences in white matter lesion burden between paired combinations of the groups.

Results

Conventional MR imaging findings

Mild or moderate diffuse brain atrophy was present in 33 % of the SLE and NPSLE patients (13/39) and in 1 of the 19 HC. None of the patients had acute ischemia. One SLE patient had a wedge shaped area of encephalomalacia in the right frontal lobe and one NPSLE patient had an old infarct in the right frontal lobe. A mild lesion burden, as defined above, was seen in 72 % of the SLE patients (13/18), a moderate burden was present in 16.7% (3/18), and a severe burden in 5.6% (1/18). One of the 21 NPSLE patients had no lesions (4.8%); a mild lesion burden was seen in 57.1% of the NPSLE patients (12/21), a moderate burden in 23.8% (5/21), and a severe burden in 14.3% (3/21). In the HC group, 6 participants (31.6%) had a mild lesion burden, 1 participant (5.3%) had a moderate burden and 1 participant (5.3%) had a severe burden. The white matter burden was significantly different between the HC and the SLE and NPSLE patients. White matter burden were significantly lower in HC versus SLE ($p<0.05$) and in HC versus NPSLE ($p<0.05$), while no significant differences in white matter burden were present between SLE and NPSLE patients. In addition some incidental findings were noted: 7 venous angiomas, 3 pineal cysts, 2 arachnoid cysts, one small meningioma, and one aneurysm of the right carotid artery.

MR perfusion findings

The overall relative cerebral blood flow (CBF) (combining all 9 ROI) was significantly increased in the SLE patients compared to healthy controls, the significant differences between these two cohorts was most striking in the following areas: right posterior thalamus, right hypothalamus, posterior cingulate gyrus, and the left parahippocampal gyrus (as summarized in table 3).

Similarly, the overall CBV was increased in SLE patients compared to healthy controls in all sampled regions (1.40 ± 0.49 vs 1.25 ± 0.46 , $p=0.1$), and significantly so in the left hypothalamus region (1.17 ± 0.34 vs 0.94 ± 0.31 , $p=0.048$).

Although not statistically significant, the NPSLE patients showed overall decreased CBF compared to the SLE patients within each brain region (1.39 ± 0.44 vs 1.45 ± 0.40), and the HC cohort had overall lower CBF than the NPSLE patients (1.32 ± 0.37 vs 1.39 ± 0.44).

The CBV of the NPSLE patients showed significantly higher variability (SD=0.65) than both the SLE patients (SD=0.49) and HC patients (SD=0.47), ($p=0.0004$ and $p<0.0001$, respectively). Additionally, the CBF in the NPSLE patients showed higher variability (SD=0.44) compared to the CBF in the HC group (SD=0.37), ($p = 0.03$). The SLE patients had higher variability (SD= 0.40) compared to the HC cohort (SD=0.37), but this difference was not statistically significant.

No statistically significant MTT differences were seen in the NPSLE, SLE, or HC cohorts.

MR perfusion and clinical/laboratory data

Eighteen diffuse neuropsychiatric manifestations and 7 focal manifestations were present in the NPSLE group. The following manifestations were seen: 3 psychosis, 1 transverse myelitis, 10 acute confusional state, 3 headaches, 1 depression, 6 cerebrovascular disease, and 1 cranial nerve deficit. The majority of the patients (20/21) were acutely treated with intravenous and/or oral steroids. One patient was treated with SSRIs alone. Thirteen patients required the addition of immunosuppressive drugs as well.

There was a significantly positive correlation ($r = 0.53$, $p\text{-value} = 0.02$) between the SLEDAI score and the CBV and MTT ($r = 0.61$, $p\text{-value} = 0.01$) in the posterior cingulate gyrus of SLE patients. These correlations were not observed in the NPSLE or HC group. A positive correlation was also seen between the anti-double stranded DNA antibody and the CBF for the posterior cingulate gyrus ($r = 0.54$, $p\text{-value} = 0.02$).

SLE patients (2.1 ± 2.5) had significantly lower SLEDAI scores than NPSLE patients (11.3 ± 6.2); $p < 0.01$. No association was found between MR perfusion measurements and the anti-cardiolipin antibodies.

Discussion

The diagnosis of NPSLE is challenging and currently lacks a biologic or radiographic marker for disease. In our study, we were unable to distinguish NPSLE patients from SLE or HC patients based solid on the dynamic susceptibility contrast enhanced MRI (i.e. based on perfusion images). Our findings are in agreement with a similar study by Emmer et. al., which looked at larger areas of subcortical grey matter and central white matter and thalamus using larger ROI's than in the present study and also did not find any statistically significant MR perfusion abnormalities in NPSLE patients compared to SLE and HC patients⁹.

We did not find a diagnostic MR perfusion target in NPSLE patients, but noted that these patients had significantly increased variability in cerebral blood flow and volume compared to the SLE and HC patients. This significantly increased variability in CBF and CBV seen in NPSLE patients might partially explain why no significant changes in perfusion measures in NPSLE patients have been seen in previous studies and why researchers are struggling to find a specific diagnostic target for NPSLE^{9,15,16}. Perhaps multiple concordant targets are necessary, or alternatively the diagnosis of NPSLE is too broad, and if narrowed, might render a clearer diagnostic tool.

One possibility would be to evaluate patients who fit the American College of Rheumatology case definition for NPSLE, and then exclude the patients with common symptoms seen in healthy patients such as: headache, mild anxiety, depression, polyneuropathy (without electrophysiologic confirmation) and mild cognitive dysfunction, which would increase the specificity from 46% to 93%^{17,18,19}.

Our SLE patients showed significantly increased CBF and CBV compared to HC, which was also seen in a dynamic susceptibility contrast enhanced MRI study by Gasparovic et. al.⁷ Specifically, we found that the CBF was significantly increased in five brain areas: right posterior thalamus, right hypothalamus, left parahippocampal gyrus, posterior cingulate gyrus, and left hypothalamus in the SLE patients compared to healthy controls. Although there is no vascular territory or function to link these structures, our results are in agreement with others that have found that SLE patients have patchy increased cerebral blood flow compared to healthy controls^{7,21,22, 23}.

We found, in contradiction to some previous MR and SPECT studies^{9, 15,16, 24} that SLE patients with signs of active disease (increased anti-double stranded DNA antibodies and increased SLEDAI scores) showed statistically increased CBF, CBV, and MTT in the posterior cingulate gyrus.

Why the posterior cingulate gyrus? One potential explanation is that the posterior cingulate gyrus is near the circumventricular organs (namely the pineal gland and the subcommissural organ). The circumventricular organs have incomplete blood brain barriers therefore inflammatory substances in the bloodstream can freely move into the CSF through these organs. It stands to reason that serum inflammatory markers in lupus would be most concentrated in the CSF around these organs, two of which happen to be adjacent to the posterior cingulate gyrus.

One potential limitation of this paper is that we used relative perfusion measurements, which are generated by dividing all CBV, CBF, and MTT values by a reference tissue, in our case, the normal appearing frontal white matter. Although this is common practice in creation and interpretation of MR perfusion studies, this method implies the perfusion of the frontal white matter is normal, which may not be the case in patients with lupus. Gasparovic et. al. did not normalize perfusion values by using a “normal appearing” tissue as a denominator, and found that SLE patients had increased CBF and CBV compared to HC⁷.

Along the same lines, we used the right middle cerebral artery as the arterial input function, assuming it would be an accurate indicator of arterial input. However, any arterial delay encountered between the right middle cerebral artery and the region of interest introduces error to the CBF measurements²³. The mean age of our subjects was 44, which is similar to other studies^{8,9} therefore if atherosclerotic disease is a cofounder it is a shared cofounder. Gadolinium was injected at 2 cc/sec, which is a slow rate, but was held constant for all patients in the study.

Furthermore, we presume in this study that the patients who have been categorized as “NPSLE” patients were appropriately diagnosed by the American College of Rheumatology criteria recognizing that it is possible that some of our “SLE” patients might present with NPSLE symptoms at a later date.

Conclusion

In conclusion, we found that SLE patients had statistically increased cerebral blood flow and cerebral blood volume in specific brain locations and as a whole compared to NPSLE and HC patients. The SLE patients with clinical findings suggestive of active disease (elevated SLEDAI scores and anti-dsDNA) displayed statistically significant increased blood flow, volume, and mean transit time in the posterior cingulate gyrus. We also found that NPSLE patients had significantly increased variability in the CBF and CBV measures compared to SLE patients and HC subjects.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Bruyn GA. Controversies in lupus: Nervous system involvement. *Ann Rheum Dis.* 1995 Mar; 54(3): 159–167. [PubMed: 7748011]
2. Kovacs JA, Urowitz MB, Gladman DD. Dilemmas in neuropsychiatric lupus. *Rheum Dis Clin North Am.* 1993; 19(4):795–814. [PubMed: 8265823]
3. Bertias GK, Ioannidis JPA, Aringer M, et al. EULAR recommendations for the management of systemic lupus erythematosus with neuropsychiatric manifestations: Report of a task force of the EULAR standing committee for clinical affairs. *Ann Rheum Dis.* 2010; 69(12):2074–2082. [PubMed: 20724309]
4. Hanly J, McCurdy G, Fougere L, et al. Neuropsychiatric events in systemic lupus erythematosus: Attribution and clinical significance. *J Rheumatol.* 2004; 31(11):2156–2162. [PubMed: 15517627]
5. Harel L, Sandborg C, Lee T, et al. Neuropsychiatric manifestations in pediatric systemic lupus erythematosus and association with antiphospholipid antibodies. *J Rheumatol.* 2006; 33(9):1873–1877. [PubMed: 16845706]
6. Bernatsky S, Clarke A, Gladman DD, et al. Mortality related to cerebrovascular disease in systemic lupus erythematosus. *Lupus.* 2006; 15(12):835–839. [PubMed: 17211987]
7. Gasparovic C, Roldan C, Sibbitt W, et al. Elevated cerebral blood flow and volume in systemic lupus measured by dynamic susceptibility contrast magnetic resonance imaging. *J Rheumatol.* 2010; 37(9):1834–1843. [PubMed: 20551095]
8. Borrelli M, Tamarozzi R, Colamussi P, et al. Evaluation with MR, perfusion MR and cerebral flowSPECT in NPSLE patients. *Radiol Med.* 2003 May-Jun;105(5–6):482–489. [PubMed: 12949459]
9. Emmer B, van Osch M, Wu O, et al. Perfusion MRI in neuro-psychiatric systemic lupus erythematosus. *Journal of magnetic resonance imaging.* 2010; 32(2):283–288. [PubMed: 20677252]
10. Hochberg MC. Updating the american college of rheumatology revised criteria for the classification of systemic lupus erythematosus. *Arthritis rheumatism.* 1997; 40(9):1725. [PubMed: 9324032]
11. Mouannes-Srour JJ, Shin W, Ansari SA, et al. Correction for arterial-tissue delay and dispersion in absolute quantitative cerebral perfusion DSC MR imaging. *Magn Reson Med.* 2011 Dec 12.
12. Sundgren PC, Jennings J, Attwood JT, et al. MRI and 2D-CSI MR spectroscopy of the brain in the evaluation of patients with acute onset of neuropsychiatric systemic lupus erythematosus. *Neuroradiology.* 2005; 47(8):576–585. [PubMed: 16007461]
13. Folstein MF, Folstein SE, McHugh PR. “Mini-mental state”: A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res.* 1975; 12(3):189–198. 11. [PubMed: 1202204]
14. Gladman D, Ginzler E, Goldsmith C, et al. The development and initial validation of the systemic lupus international collaborating Clinics/American college of rheumatology damage index for systemic lupus erythematosus. *Arthritis rheumatism.* 1996; 39(3):363–369. [PubMed: 8607884]

15. Waterloo K, Omdal R, Sjöholm H, et al. Neuropsychological dysfunction in systemic lupus erythematosus is not associated with changes in cerebral blood flow. *J Neurol*. 2001; 248:595–602. [PubMed: 11518002]
16. Rubbert A, Marienhagen J, Pierner K, et al. Single-photon-emission computed tomography analysis of cerebral blood flow in the evaluation of central nervous system involvement in patients with systemic lupus erythematosus. *Arthritis Rheum*. 1993; 36:1253–1262. [PubMed: 8216419]
17. Ainiala H, Hietaharju A, Loukkola J, et al. Validity of the new american college of rheumatology criteria for neuropsychiatric lupus syndromes: A population-based evaluation. *Arthritis rheumatism*. 2001; 45(5):419–423. [PubMed: 11642640]
18. Hanly J, Su L, Farewell V, et al. Prospective study of neuropsychiatric events in systemic lupus erythematosus. *J Rheumatol*. 2009; 36(7):1449–1459. [PubMed: 19447937]
19. Hanly JG, Urowitz MB, Su L, Bae SC, et al. Prospective analysis of neuropsychiatric events in an international disease inception cohort of patients with systemic lupus erythematosus. *Ann Rheum Dis*. 2010; 69(3):529–535. [PubMed: 19359262]
20. Lee P, Joo U, Bang O, Seo C. Basal ganglia hyperperfusion in a patient with systemic lupus erythematosus-related parkinsonism. *Neurology*. 2004; 63(2):395–396. [PubMed: 15277652]
21. Khubchandani RP, Viswanathan V, Desai J. Unusual neurologic manifestations (I): Parkinsonism in juvenile SLE. *Lupus*. 2007; 16(8):572–575. [PubMed: 17711890]
22. Emmi L, Bramati M, De Cristofaro MT, et al. MRI and SPECT investigations of the CNS in SLE patients. *Clin Exp Rheumatol*. 1993; 11(1):13–20. [PubMed: 8453792]
23. Calamante F, Gadian DG, Connelly A. Quantification of perfusion using bolus tracking magnetic resonance imaging in stroke: Assumptions, limitations, and potential implications for clinical use. *Stroke*. 2002; 33(4):1146–1151. [PubMed: 11935075]
24. Nossent JC, Hovestadt A, Schonfeld DH, et al. Single-photon-emission computed tomography of the brain in the evaluation of cerebral lupus. *Arthritis Rheum*. 1991; 34:1397–1403. [PubMed: 1953818]
25. Bombardier C, Gladman DD, Urowitz MB, et al. Derivation of the SLEDAI. A disease activity index for lupus patients. the committee on prognosis studies in SLE. *Arthritis rheumatism*. 1992; 35(6):630–640. [PubMed: 1599520]

Figure 1.
Axial MR perfusion images show the locations of the regions of interest.

Table 1

Demographic and Clinical Data

	HC n = 19	SLE n = 18	NPSLE n = 21	p-value
	Range Mean $\pm$ SD	Range Mean $\pm$ SD	Range Mean $\pm$ SD	
Age	21.1–65.8 44.9 $\pm$ 14.3	23.5–64.7 43.1 $\pm$ 10.7	28.4–69.9 43.7 $\pm$ 11.8	0.9
Female (%)	19 (100.0%)	17 (94.4%)	21 (100.0%)	0.3
Age at disease onset	N/A	18–56 33.4 $\pm$ 10.9	13–65 32.7 $\pm$ 13.5	0.8
Disease duration (years)	N/A	3–19 9.4 $\pm$ 5.2	2–25 10.5 $\pm$ 6.8	1.0
SLEDAI	N/A	0–8 2.1 $\pm$ 2.5	1–25 11.3 $\pm$ 6.2	< 0.01

HC = healthy controls, SLE = systemic lupus erythematosus, NPSLE, neuropsychiatric systemic lupus erythematosus, SD = standard deviation, SLEDAI = systemic lupus erythematosus disease activity index

Table 2

Clinical components of the SLE disease activity index (SLEDAI), which are tallied for the final score.²⁵

<u>SLEDAI score</u>	<u>symptom</u>
8	seizure
8	psychosis
8	organic brain syndrome
8	visual disturbance
8	cranial nerve disorder
8	lupus headache
8	stroke
8	vasculitis
4	arthritis
4	myositis
4	urinary casts
4	hematuria
4	proteinuria
4	pyuria
2	new rash
2	alopecia
2	mucosal ulcers
2	pleurisy
2	pericarditis
2	low complement
2	increased DNA binding
1	fever
1	thrombocytopenia
1	leukopenia

Table 3

Relative Cerebral Blood Flow: SLE versus healthy controls

	SLE	HC	p-value
	Mean $\pm$ SD	Mean $\pm$ SD	
Overall (all brain regions)	1.45 $\pm$ 0.40	1.32 $\pm$ 0.37	0.01
Right posterior thalamus	1.50 $\pm$ 0.19	1.35 $\pm$ 0.21	0.03
Right hypothalamus	1.22 $\pm$ 0.22	1.07 $\pm$ 0.24	0.042
Posterior cingulate gyrus	1.58 $\pm$ 0.27	1.42 $\pm$ 0.23	0.048
Left parahippocampalgyrus	1.78 $\pm$ 0.30	1.6 $\pm$ 0.26	0.042

SLE = systemic lupus erythematosus, HC = healthy controls, SD = standard deviation