

Cerebral small vessel disease burden is increased in lupus

The chronic inflammatory disease lupus can involve the brain, including increasing stroke risk for reasons which are not fully understood. Cerebral small vessel disease (SVD) is a disease of the blood vessels in the brain that can lead to stroke. We were interested in whether patients with lupus had features of SVD on brain imaging, as a way of helping us to understand how the brain might be affected in lupus. The known features of SVD on brain images include white matter hyperintensities (WMH) and visible perivascular spaces (PVS). Our aims were to measure and compare imaging biomarkers of SVD in patients with lupus with healthy controls that did not have lupus, and patients with minor stroke.

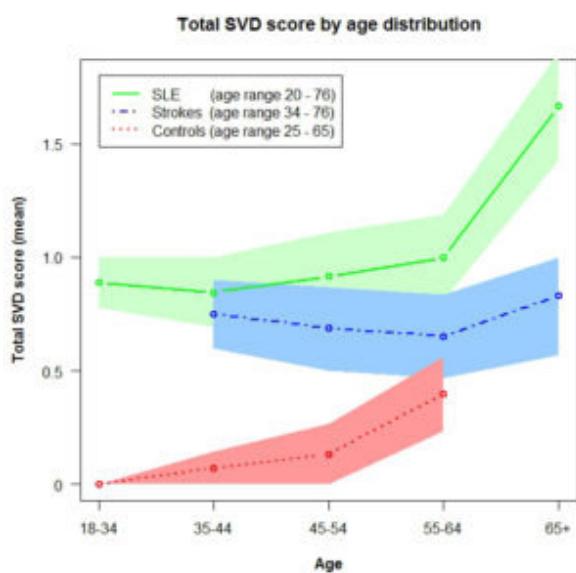


Fig. 1. Total SVD score by age distribution in lupus (SLE), stroke and healthy controls.

This was a brain magnetic resonance imaging (MRI) study that recruited patients with lupus between April and December 2014. The lupus clinic reviews all patients diagnosed with lupus in one health region from the point of diagnosis onwards. We recruited as consecutively as possible and patients represented a wide range of lupus, being of varying disease durations and severities. All patients were seen by a consultant rheumatologist. The project received research ethics committee approval (14/SS/0003) and all participants gave written informed consent.

We obtained control data from healthy volunteers aged between 25 and 65 years, recruited by poster campaign at the same health region. We also compared lupus patients to patients with first-ever minor stroke, recruited from the same health region via the regional stroke service. A stroke specialist determined the stroke type and this was confirmed by MRI.

Medical histories including smoking status, high blood pressure and diabetes were recorded. Blood was taken to measure various molecules, including the level of inflammation. Lupus disease activity was

assessed by an experienced rheumatology nurse specialising in lupus who interviewed each patient and had access to all medical data and blood results. We used routine tools to assess cognitive abilities as well as anxiety and depression as these can be affected in lupus. All patients and controls had an MRI scan of the brain.

All MRI scans were reviewed by a consultant. WMH and PVS were assessed and quantified. The amount of brain tissue was calculated. A total SVD score from 0–4 was calculated from the MRI scans.

	SLE	Stroke	
	N (%) or mean (SD) or median (Q1–Q3)	N (%) or mean (SD) or median (Q1–Q3)	p value
N	51	51	
Females (n)	47 (92%)	47 (92%)	0.99
Age (years)	48.8 (14.3)	55.3 (8.9)	0.008
Disease duration (months)	50 (24–148)	NA	NA
Members of SLEx registry	31 (61%)	NA	NA
NPSLE	4 (8%)	NA	NA
BMI (kg / m ²)	29 (6.5)	NA	NA
Current smoker	6 (12%)	28 (54.9%)	<0.0001
Hypertension	9 (18%)	32 (62.7%)	<0.0001
Diabetes	None	2 (3.9%)	NA
Past medical history of stroke	1 (1.9%)	51	NA
Current steroids	18 (35%)	NA	NA
Fatigue (score)	5.0 (1.7)	NA	NA
MMSE (score, max 30)	28 (27–30)	NA	NA
MoCA (score, max 30)	26 (24–28)	NA	NA
ACER (score, max 100)	91 (87–94)	NA	NA
SLICC (score)	0 (0–1)	NA	NA
SLEDAI-2K (score)	2 (0–4)	NA	NA
BILAG (score)	2 (1–9)	NA	NA

ACER = Addenbrooke's Cognitive Examination – Revised, BMI = body mass index, BILAG = British Isles Lupus Assessment Group, MMSE = Mini Mental State Examination, MoCA = Montreal Cognitive Assessment, NPSLE = neuropsychiatric SLE, NA = not applicable, SLE = systemic lupus erythematosus, SLEx = Scottish Lupus Exchange Registry, SLEDAI-2K = systemic lupus erythematosus Disease Activity Index, SLICC = Systemic Lupus International Collaborating Clinics

Tab. 1. Subject characteristics.

We contacted 55 patients with lupus and 51 agreed to take part. There were 47 women and 4 men and the average age was 49 years old (the youngest was 20 years, the oldest 76 years). Clinical data are given in Table 1. Healthy controls were of similar age while the stroke patients were on average six years older than the lupus patients. There were more smokers and patients with high blood pressure in the stroke group.

WMHs were seen in 49/51 (96%) and 36/51 (70%) lupus patients respectively. All lupus patients had visible PVS. Compared to healthy controls, lupus patients had a greater total SVD score (Tab. 2) sustained across each 10-year age band (Fig. 1), including more WMHs. Compared to stroke patients, the lupus patients also had a higher total SVD score, mostly due to having more PVS. The total SVD score was not associated with SLE activity, cognitive abilities, lupus disease duration or any blood measure.

	Group			Kruskal-Wallis Group p value	Pairwise posttest p value		
	SLE (n=51)	Stroke (n=51)	Controls (n=51)		SLE – Stroke	SLE – Controls	Stroke – Controls
Lacunes	0 (0–0)	0 (0–0)	0 (0–0)	0.02			0.01
Microbleeds	0 (0–0)	0 (0–0)	0 (0–0)	0.15			
PVS BG (score 0–4)	2 (2–3)	1 (1–1)	1 (1–1)	<0.0001	<0.0001	<0.0001	
PVS CS (score 0–4)	3 (3–4)	1 (1–2)	1 (1–1)	<0.0001	<0.0001	<0.0001	0.001
WMH periventricular (score 0–3)	1 (1–1)	1 (1–1)	1 (1–1)	0.48			
WMH deep (score 0–3)	1 (0–1)	1 (0.5–1)	0 (0–1)	<0.0001		0.01	0.0007
WMH (total Fazekas score 0–6)	2 (1–2)	2 (1–2.5)	1 (1–2)	0.02		0.05	0.03
Total SVD score (score 0–4)	1 (1–1)	0 (0–1)	0 (0–0)	<0.0001	0.02	<0.0001	0.0006
Deep atrophy (score 1–6)	1 (1–2)	1 (1–1)	1 (1–2)	0.14			
Superficial atrophy (score 1–6)	1 (1–2)	1 (1–1)	1 (1–1)	0.006		0.004	

Values are medians (Q1–Q3). The p value compares the individual SVD features across the three groups by Kruskal-Wallis test. Posttest comparisons identifies where differences exists. Blank cells = non-significant. BG=basal ganglia, CS=centrum semiovale, PVS=perivascular spaces, SVD=small vessel disease, SLE=systemic lupus erythematosus, WMH=white matter hyperintensities.

Tab. 2. Imaging biomarkers of SVD in SLE patients, healthy controls and stroke patients.

An analysis of the brain scans showed the lupus group had more brain imaging evidence of SVD compared with healthy controls. We also compared the group of lupus patients with a group of patients that had already suffered a minor stroke. In this comparison we found similar levels of SVD generally between the groups and even more of some SVD features in the lupus group. We concluded a larger study was needed to confirm our findings.

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