

real-time videomicroscopy to capture high velocity events and an unbiased computer assisted analysis approach, we provide images and quantifications of the cellular responses downstream of Fc γ RIIA stimulation. We observed platelet aggregation and neutrophil adhesion to blood vessel walls in response to ICs, only in Fc γ RIIA^{TGN} mice. Moreover, stable and transient interactions between platelets and neutrophils were captured in real time. Taken together, the results highlight the importance of the Fc γ RIIA receptor in neutrophil adhesion to the BBB in response to ICs and suggest the potential implication of neutrophils and platelets in mediating alterations of the BBB in NPSLE. This study puts forward an imaging and quantifying approach in a quadruple transgenic mouse model that can be utilized for the study of the pathogenic roles of ICs disease.

405

STRUCTURAL NEURAL UNDERPINNINGS OF LOW MOOD AND ANXIETY IN CHILDHOOD ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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10.1136/lupus-2022-lupus21century.17

Objectives Emotional dysfunction in childhood-onset systemic lupus erythematosus (cSLE) impacts clinical outcomes and quality of life, but the relationship to lupus brain inflammation is poorly understood. We aimed to investigate the structural neural metrics and disease activity measures that predict anxiety and depression in cSLE and non-cSLE children.

Methods A cross-sectional sample of patients with cSLE (meeting ACR and/or SLICC classification criteria for SLE) and healthy controls, aged 10-17 years completed self-reported measures of depression (Beck Depression Inventory-II/Children's Depression Inventory-2) and anxiety (Screen for Child Anxiety Related Disorders). Elevated depression/anxiety symptoms were determined by established clinical cut-offs. T1-weighted sequences were acquired on a 3T Siemens MRI. MRI scans were spatially normalized using the MNI-152 template, and grey and white matter were segmented to estimate brain volume, surface area and cortical thickness in Freesurfer. Measures of disease duration, activity (SLE Disease Activity Index (SLEDAI) 2000), glucocorticoid use and inflammation were collected. Partial least squares (PLS) analyses were used to investigate the association between structural brain metrics and disease measures with depression/anxiety symptom severity.

Results Twenty-seven patients with cSLE (mean age=15.4 years (SD 1.7) and median SLEDAI=2.0 (IQR 2-4)) and 14 healthy controls were recruited. There were no group differences in age, sex or ethnicity. Median cumulative glucocorticoid use in this sample was 3.2 grams prednisone-equivalent (IQR 0.7-11.2). One cSLE patient had a history of neuropsychiatric lupus. We did not find group differences in prevalence of clinically elevated depression (cSLE= 12/27, controls=6/14) or anxiety (cSLE= 11/27, controls=7/14). Within group analysis

of brain MRI showed that for both cSLE patients and controls, worse mood and anxiety were both predicted by reduced right anterior cingulate thickness. Within the cSLE group, worse mood and anxiety was predicted by higher cumulative steroid use, reduced right fusiform gyrus cortical thickness, and increased left amygdala and right parahippocampal volumes and thickness.

Conclusion This cross-sectional sample of cSLE patients had mild disease activity at the time of the study, and a high but similar prevalence of emotion problems compared to controls. Worse emotional functioning was associated with altered structural changes in regions known to underlie emotion processing in both groups. Emotion difficulties in the cSLE group were related to cumulative glucocorticoid use, but not disease activity or inflammatory markers. Further research is needed to examine the role of glucocorticoid exposure in the setting of psychological stress related to having a chronic illness during the adolescent neurodevelopmental period.

Lay Summary Children with lupus often experience problems with mood, such as depression and anxiety. These problems may be due to the effects of lupus on the brain, but the cause is currently unclear. We measured symptoms of depression and anxiety in 30 children with lupus. We also used advanced brain imaging to study changes in brain structure. We compared these measures between children with lupus and a group of 14 health peers. We also looked at how mood problems are related to brain imaging changes and lupus disease markers. Compared to their peers, we found that children with lupus had similar rates of depression and anxiety symptoms. We found that these symptoms were related to changes in brain structure in both children and their peers. In children with lupus, the symptoms were related to changes in particular brain areas. Depression and anxiety were also related to higher steroid use. These findings indicate that depression and anxiety symptoms are common in children with lupus and their peers. The results also suggest that these mood problems correlate with changes in the brain, and with steroid treatment for lupus. More research is needed to understand how steroid treatment impacts brain and mental health in children with lupus. This will lead to better mental health and overall care for these children.

501

ROLE OF PLATELET-BOUND COMPLEMENT ACTIVATION PRODUCT (PC4D) IN PREDICTING RISK OF FUTURE THROMBOTIC EVENTS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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10.1136/lupus-2022-lupus21century.18

Background Platelet-bound complement activation products (PC4d) are associated with a history of thrombosis in systemic lupus erythematosus (SLE) (Gartshteyn et al., 2021; Petri et al., 2017). The current study evaluated the role of PC4d in assessing the risk of future thrombosis.

Methods PC4d (expressed at net mean fluorescence intensity [MFI]) was measured by flow cytometry from patients enrolled in the Lupus Cohorts at Columbia Univ (COL), Johns Hopkins Univ (JH) and Beth Israel Deaconess Medical Center (BI) between Apr-Sep 2017 (JH), Aug 2018-Jan 2020

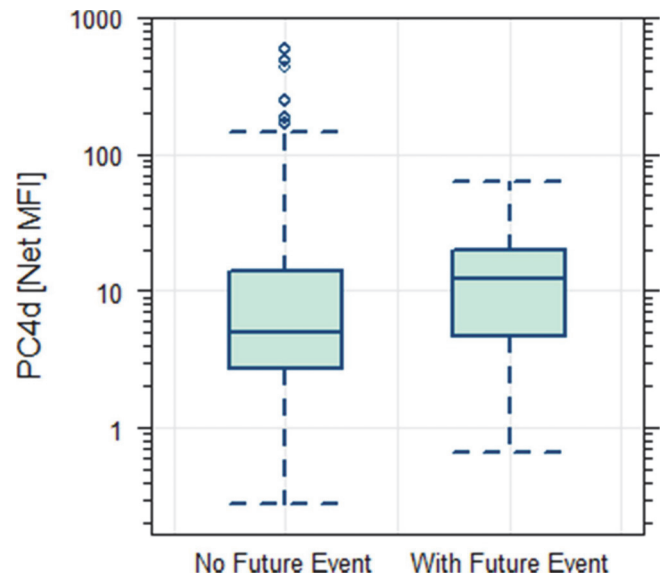
Abstract 501 Table 1 Demographic characteristics of the patients in the 3 cohorts and overall. Data is reported as number (n) and percentages (%). Anti-phospholipid (aPL) positivity was based on positivity for any of the isotypes: anti-phosphatidylserine/prothrombin complex (PS/PT) IgG or IgM, anti-cardiolipin (aCL) IgG, IgM, or IgA, and anti-beta2-glycoprotein1 (aB2GP1) IgG, IgM, or IgA.

	JH	COL	BI	Total
N	149	150	120	419
Female; n (%)	128 (86%)	137 (91%)	98 (82%)	363 (87%)
Age, years; median (IQR)	48 (36-59)	38 (30-47)	36 (28-49)	41 (31-53)
Younger than < 65 years old at	127 (85%)	139 (93%)	117 (98%)	383 (91%)
PC4d measurement; n (%)				
Ethnicity; n (%)				
African	51 (34%)	39 (26%)	37 (31%)	127 (30%)
Asian	6 (4%)	14 (9%)	15 (13%)	35 (8%)
Caucasian	83 (56%)	40 (27%)	52 (43%)	175 (42%)
Hispanic	0 (0%)	49 (33%)	0 (0%)	49 (12%)
Other	9 (6%)	3 (3%)	3 (3%)	15 (4%)
Not available	0 (0%)	5 (3%)	13 (11%)	18 (4%)
aPL positivity; n (%)				
aPS/PT or aCL or aB2GP1	80 (54%)	64 (43%)	42 (35%)	186 (44%)
aPS/PT	72 (48%)	44 (29%)	35 (29%)	151 (36%)
aCL	39 (26%)	30 (20%)	15 (12%)	84 (20%)
aB2GP1	36 (24%)	34 (23%)	14 (12%)	84 (20%)

(COL), and Oct 2018-Mar 2022 (BI). History of thrombotic vascular events was confirmed by medical record review. Data were analyzed by chi-square and logistic regression. Diagnostic odds ratio (DOR) was calculated. If a patient had 2 arterial or 2 venous events, only the closest in time to PC4d measurement was included in the analysis.

Results A total of 419 SLE patients were enrolled. Main demographic and clinical characteristics are in table 1. Seventy-four thrombotic events occurred in the 5 years pre- to 3 years post-PC4d measurement. Of these 74, 50% had PC4d \geq 10 MFI at enrollment while 72% of patients without thrombosis had PC4d<10 ($p < 0.001$). 19 events occurred in 15 subjects in the 3 years after PC4d measurement: 8 cerebrovascular accidents, 3 deep vein thrombosis, 2 gastrointestinal infarctions, 2 myocardial infarctions, 1 pulmonary infarction, 1 arterial thrombosis and 2 venous thrombosis not specified. Median PC4d was higher in the 15 patients with than in the 404 patients without thrombosis (12.2 MFI, IQR: 4.7-19.6 vs. 4.9 MFI, IQR: 2.6-13.6, $p = \text{NS}$) (figure 1).

When the arterial events closest to PC4d measurements (8 of 14 total arterial events) were included, PC4d>13 MFI had sensitivity=62%, specificity=74%, DOR=4.8 (95%CI: 1.1, 20.3), $p = 0.034$ in predicting future arterial thrombosis in patients with a previous arterial thrombosis. As expected, a previous arterial thrombosis was a strong predictor of a subsequent arterial event ($p = 0.0042$). PC4d \geq 10 or \geq 20 MFI did not reach statistical significance for future thrombosis neither in the entire population ($p = 0.055$ and 0.51 , respectively) nor in the subgroup younger than 65 years old ($p = 0.99$ for both). However, the negative predictive value of PC4d<10 MFI was 98%, indicating that probability of not having a thrombosis within 3 years is 98% if PC4d<10 MFI. Of the 285 patients with PC4d<10 MFI, 105 (37%) were positive for at least 1 of 8 anti-phospholipid antibodies (aPL) (3 aCL, 3 anti-B2GP1, or 2 anti-PS/PT antibodies), and 22 (7.8%) were positive for 3 aPL, indicating that the



Abstract 501 Figure 1 Box and whisker plot with PC4d levels (net MFI) in patients who experienced (right) or not (left) thrombotic events post-PC4d measurement.

probability of not having a thrombosis if PC4d<10 MFI holds true for the population aPL positive and presumed at higher risk.

Conclusions PC4d \geq 10 MFI is associated with thrombosis in SLE and predicts future arterial thrombosis (DOR=4.8), despite the small number of events post-PC4d. Interestingly, patients with PC4d < 10 MFI have a 98% probability of not experiencing a thrombotic event in the following 3 years. Taken together, these findings suggest that PC4d levels help evaluate the risk of thrombosis in SLE and can guide the decision to start low dose aspirin.