

1 **Supplementary files**2 **Supplementary table 1** NPSLE syndromes (1999 ACR case definitions) present at baseline, other

3 than cognitive dysfunction

NPSLE	
<i>(n = 36)</i>	
1999 ACR NPSLE syndromes	
<i>(n, %)</i>	
Aseptic meningitis	1 (3)
Cerebrovascular disease	12 (31)
Demyelinating syndrome	0 (0)
Headache	3 (8)
Movement disorder	2 (6)
Myelopathy	3 (8)
Seizure disorder	3 (8)
Acute confusional state	3 (8)
Anxiety disorder	0 (0)
Mood disorder	5 (14)
Psychosis	3 (8)
AIDP	0 (0)
Autonomic disorder	0 (0)
Myasthenia gravis	0 (0)
Cranial neuropathy	3 (8)
Mononeuropathy	0 (0)
Polyneuropathy	0 (0)
Plexopathy	2 (6)
Other*	4 (11)

4 * Other NPSLE syndromes: organic brain syndrome (n = 2), lethargia (n = 1), walking disorder (n = 1).

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6 AIDP = acute inflammatory demyelinating polyneuropathy; NPSLE = neuropsychiatric systemic lupus

7 erythematosus.

8 **Supplementary table 2** Raw test scores and Z-scores per cognitive domain in patients with different
9 NPSLE phenotypes

	All patients (n = 151)	Minor/non- NPSLE (n = 115)	Inflammatory NPSLE (n = 24)	Ischemic NPSLE (n = 12)
Global cognitive function				
<u>Raw score</u>				
MMSE (total)	29 [14 – 30]	29 [14 – 30]	28 [22 – 30]	28 [25 - 30]
<u>Z-score*</u>	0.00 ± 1.00	0.07 ± 0.97	-0.32 ± 1.19	-0.04 ± 0.82
Learning & memory				
<u>Raw score</u>				
Wechsler memory scale (total) †	58.13 ± 12.15	59.13 ± 10.70	53.39 ± 17.95	58.00 ± 9.47
<u>Z-score</u>	0.04 ± 0.91	0.08 ± 0.87	-0.17 ± 1.11	0.07 ± 0.79
Executive function & complex attention				
<u>Raw score (time in seconds)</u>				
STROOP card 3	104.87 ± 39.20	104.65 ± 39.74	114.80 ± 42.43	87.20 ± 17.31
TMT B	76 [26 – 349]	76 [26 – 349]	87 [46 – 318]	70 [47- 270]
<u>Z-score</u>	-0.06 ± 0.96	-0.05 ± 0.19	-0.28 ± 1.03	0.19 ± 0.89
Psychomotor speed				
<u>Raw score (time in seconds)</u>				
STROOP card 1	48 [33 – 115]	48 [34 – 115]	51 [33 – 71]	46 [37 – 54]
STROOP card 2	66.17 ± 17.28	65.77 ± 16.28	72.62 ± 22.71	56.50 ± 6.55
TMT A	39.51 ± 18.32	39.19 ± 18.00	42.79 ± 20.96	35.92 ± 16.10
<u>Z-score</u>	-0.07 ± 0.94	-0.08 ± 0.95	-0.21 ± 0.98	0.22 ± 0.78

10 Data represents mean ± SD or median [range].

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12 *The Z-score represents the average number of standard deviations from the mean value of the total population

13 of the patients of the NPSLE clinic included in this study. † Total Wechsler Memory Scale score before age

14 correction.

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16 NPSLE = neuropsychiatric systemic lupus erythematosus; TMT = Trail Making Test.

17 **Secondary analyses**18 **Supplementary table 3** Association between cognitive function and brain and white matter

19 hyperintensity (WMH) volume in patients with different (NP)SLE phenotypes, additionally adjusted for

20 presence of diabetes and hypertension

	Global cognitive function		Learning & memory		Executive function & complex attention		Psychomotor speed	
	B	95% CI	B	95% CI	B	95% CI	B	95% CI
<i>All patients (n = 151)</i>								
Total brain volume	0.00*	(0.00; 0.01)	0.00*	(0.00; 0.01)	0.00*	(0.00; 0.01)	0.01*	(0.00; 0.01)
Grey matter volume	0.01*	(0.00; 0.01)	0.01*	(0.00; 0.01)	0.01*	(0.00; 0.01)	0.01*	(0.00; 0.01)
White matter volume	0.00	(-0.00; 0.01)	0.00*	(0.00; 0.01)	0.01*	(0.00; 0.01)	0.01*	(0.00; 0.01)
WMH volume [±]	-0.08	(-0.22; 0.06)	-0.08	(-0.20; 0.04)	-0.13	(-0.26; 0.00)	-0.17*	(-0.29; -0.05)
<i>Minor/non-NPSLE</i>								
Total brain volume	0.00	(-0.00; 0.01)	0.00 *	(0.00; 0.01)	0.00*	(0.00; 0.01)	0.00*	(0.00; 0.01)
Grey matter volume	0.01*	(0.00; 0.01)	0.01*	(0.00; 0.01)	0.01*	(0.00; 0.01)	0.01*	(0.00; 0.01)
White matter volume	0.00	(-0.01; 0.01)	0.00	(-0.00; 0.01)	0.01*	(0.00; 0.01)	0.01*	(0.00; 0.01)
WMH volume	0.00	(-0.16; 0.16)	-0.02	(-0.16; 0.12)	-0.07	(-0.22; 0.08)	-0.09	(-0.24; 0.07)
<i>Inflammatory NPSLE</i>								
Total brain volume	0.00	(-0.01; 0.02)	0.01	(-0.00; 0.02)	0.01	(-0.01; 0.02)	0.01	(-0.00; 0.02)
Grey matter volume	0.00	(-0.01; 0.02)	0.00	(-0.01; 0.02)	0.00	(-0.01; 0.01)	0.01	(-0.01; 0.02)
White matter volume	0.01	(-0.02; 0.03)	0.02	(-0.00; 0.03)	0.02	(-0.00; 0.04)	0.02*	(0.00; 0.03)
WMH volume	-0.17	(-0.54; 0.20)	-0.12	(-0.45; 0.21)	-0.23	(-0.56; 0.09)	-0.39*	(-0.64; -0.15)
<i>Ischemic NPSLE</i>								
Total brain volume	0.00	(-0.02; 0.01)	0.00	(-0.02; 0.02)	0.00	(-0.01; 0.01)	0.00	(-0.01; 0.01)
Grey matter volume	0.00	(-0.03; 0.03)	0.00	(-0.03; 0.03)	-0.01	(-0.01; 0.02)	0.00	(-0.01; 0.02)
White matter volume	-0.01	(-0.04; 0.04)	0.00	(-0.04; 0.04)	0.01	(-0.02; 0.03)	0.00	(-0.01; 0.03)
WMH volume	-0.02	(-1.12; 1.08)	-0.12	(-1.20; 0.95)	-0.28	(-0.94; 0.38)	-0.21	(-0.93; 0.51)

21 *These data represent B's and 95% CI's corrected for age, sex, intracranial volume, diabetes and hypertension.*22 *These values represent how much the (transformed) Z-score of a cognitive domain changes when the brain*23 *volume changes one unit. *p ≤0.05.*

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25 *NPSLE = neuropsychiatric systemic lupus erythematosus; WMH = white matter hyperintensity.*

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27 **Sensitivity analyses**

28 The cognitive domains executive function & complex attention and psychomotor speed
29 were calculated using raw scores from the Trail Making Test (TMT) and the STROOP test. In
30 our main analyses, we used a sum score of the tests that were available.

31 Because the STROOP test data for 22 patients were missing, we also performed a sensitivity
32 analysis using 1) only the TMT scores to calculate these cognitive domains, because these
33 were available for all patients and 2) only the scores of patients that completed both the
34 TMT and the STROOP test. The results are provided in *Supplementary Table 4A + 4B*.

35 **Supplementary table 4A** Sensitivity analyses comparing the cognitive domain executive function &
36 complex attention across different NPSLE phenotypes

Executive function & complex attention						
	<i>Main analysis</i>		<i>Sensitivity analysis 1[*]</i>		<i>Sensitivity analysis 2[‡]</i>	
	B	95% CI	B	95% CI	B	95% CI
Inflammatory vs minor/non-NPSLE (R)	-0.35	(-0.74;0.05)	-0.07	(-0.15; 0.04)	-0.10*	(-0.18; -0.01)
Ischemic vs minor/non-NPSLE (R)	0.42	(-0.10;0.94)	0.04	(-0.03; 0.10)	0.06	(-0.02; 0.13)
Inflammatory vs ischemic NPSLE (R)	-0.98*	(-1.56;-0.41)	-0.25*	(-0.43; -0.08)	-0.32*	(-0.50; -0.14)

37 *All B's are corrected for age, sex and education and represent how much the (transformed) Z-score of the*
38 *cognitive domain differs in the presence of a specific NPSLE phenotype. * p ≤ 0.05*

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40 ^{*}Only Trail Making Test scores used for the Z-score of executive function & psychomotor speed [‡]Only patients
41 with available Trail Making Test + STROOP included.

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43 *NPSLE = neuropsychiatric systemic lupus erythematosus; R = reference value.*

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45 **Supplementary table 4B** Sensitivity analyses comparing the cognitive domain psychomotor speed
 46 across different NPSLE phenotypes

Psychomotor speed						
	<i>Main analysis</i>		<i>Sensitivity analysis 1[†]</i>		<i>Sensitivity analysis 2[‡]</i>	
	B	95% CI	B	95% CI	B	95% CI
Inflammatory vs minor/non-NPSLE (R)	-0.24	(-0.62; 0.15)	-0.06	(-0.13; 0.01)	-0.08	(-0.17; 0.00)
Ischemic vs minor/non-NPSLE (R)	0.48	(-0.04; 0.99)	0.04	(-0.02; 0.10)	0.07	(-0.00; 0.15)
Inflammatory vs ischemic NPSLE (R)	-0.79*	(-1.41; -0.16)	-0.15	(-0.31; 0.01)	-0.26*	(-0.44; -0.08)

47 *All B's are corrected for age, sex and education and represent how much the (transformed) Z-score of the*

48 *cognitive domain differs in the presence of a specific NPSLE phenotype. * p ≤ 0.05.*

49

50 [†]Only Trail Making Test scores used for the Z-score of executive function & psychomotor speed. [‡]Only patients

51 with available Trail Making Test + STROOP included.

52 *NPSLE = neuropsychiatric systemic lupus erythematosus; R = reference value.*

53 The cognitive domain learning & memory was calculated using the total raw score of the
 54 Wechsler Memory Scale (WMS). Another possible approach is to calculate Z-scores for all
 55 the individual subscores of the WMS and then generate a combined Z-score instead of using
 56 the total raw score. This alternative approach is shown in *Supplementary Table 5*.

57 **Supplementary table 5** Sensitivity analyses comparing the cognitive domain learning & memory
 58 across different NPSLE phenotypes

	Learning & memory			
	<i>Main analysis</i>		<i>Sensitivity analysis</i> [*]	
	B	95% CI	B	95% CI
Inflammatory vs minor/non-NPSLE (R)	-0.34	(-0.71; 0.03)	-0.11*	(-0.21; -0.01)
Ischemic vs minor/non-NPSLE (R)	0.15	(-0.34; 0.64)	0.02	(-0.07; 0.11)
Inflammatory vs ischemic NPSLE (R)	-0.74*	(-1.37;-0.12)	-0.31*	(-0.55; -0.75)

59 *All B's are corrected for age, sex and education and represents how much the (transformed) Z-score of the*
 60 *cognitive domain differs in the presence of a specific NPSLE phenotype. * p ≤ 0.05.*

61 ^{*}Sensitivity analysis using the averaged Z-score of all separate components of the Wechsler Memory Scale
 62 instead of the total raw score.

64 NPSLE = neuropsychiatric systemic lupus erythematosus; R = reference value.
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