Supplementary material

Supplementary Table 1. Details of basic MR imaging parameters.

University College London Hospitals NHS Foundation Trust, UK MRIs were carried at 1.5T field strength. T2-weighted sequences were acquired in the axial plane with parameters as follows: slice thickness 5 mm, slice gap 1-2 mm, echo time 100–106 ms, repetition time 4763/6000. Axial T2*-GRE images were obtained at: repetition time 300/800 ms, echo time 40/26 ms, slice thickness 5 mm, slice gap 1.5 mm.
Cliniques Universitaires Saint Luc, Brussels, Belgium MRIs were carried at 1.5T field strength. T2-weighted sequences were acquired in the axial plane with parameters as follows: slice thickness 4-5 mm, slice gap 1 mm, echo time 89–90 ms, repetition time 4768/6040. Axial T2*-GRE sequences were acquired, with parameters as follows: repetition time 230–240 ms, echo time 50–70 ms, slice thickness 5 mm, gap 1 mm.
Addenbrooke's Hospital, Cambridge, UK MRIs were carried out at 1.5T field strength. T2-weighted sequences were acquired in the axial plane with parameters as follows: slice thickness 4-5 mm, slice gap 1-3 mm, echo time 80–100 ms. T2*-GRE sequences were obtained in the axial plane using the following parameters: repetition time 460–660 ms, echo time 15 ms, field of view 22 cm, slice thickness 6 mm, slice gap 7 mm.
CHU Mont-Godinne UCL, Belgium MRIs were carried at 1.5T field strength. T2-weighted sequences were acquired in the axial plane with parameters as follows: slice thickness 5 mm, slice gap 1-2 mm, echo time 85–100 ms, repetition time 6000. T2*-GRE sequences were obtained in the axial plane: repetition time 921 ms, echo time 22 ms, slice thickness 4 mm, slice gap 10%.

Relative distribution of EPVS in the CSO and BG between ICH categories

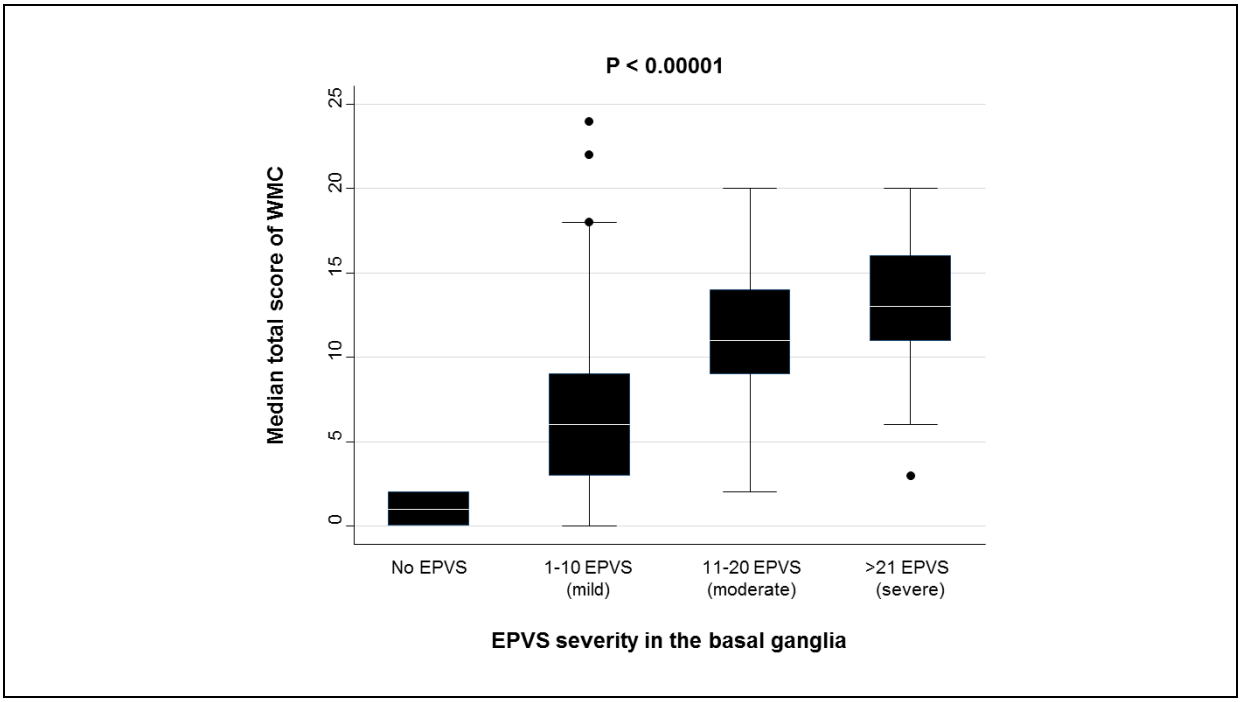
Within group comparisons of the proportion of patients with severe (>40) CSO EPVS vs. frequent-to-severe (>20) BG EPVS for strictly lobar ICH (i.e. probable and possible CAA) and other ICH showed a significance difference for strictly lobar ICH (35.5% in the CSO vs. 4% in the BG; $p<0.0001$), but no difference for the other ICH cases (17.8% in the CSO vs. 20% in the BG; $p=0.788$).

Supplementary Table 2. Associations between the severity of centrum semiovale and basal ganglia EPVS. A comparison using chi square test across categories, showed no significant relationship between EPVS severity in the two anatomical areas (p=0.100 for trend).

N (%)	**Centrum semiovale EPVS**				
Basal ganglia EPVS	Mild: 1-10	Moderate: 11-20	Frequent: 21-40	Severe: >40	*Total*
No EPVS	1 (14.29)	0 (0)	1 (2.33)	0 (0)	2 (1.65)
Mild: 1-10	2 (28.57)	23 (63.89)	21 (48.84)	24 (68.57)	70 (57.85)
Moderate: 11-20	2 (28.57)	11 (30.56)	16 (37.21)	8 (22.86)	37 (30.58)
Frequent: 21-40	2 (28.57)	2 (5.56)	5 (11.63)	2 (5.71)	11 (9.09)
Severe: >40	0 (0)	0 (0)	0 (0)	1 (2.86)	1 (0.83)
Total	7 (100)	36 (100)	43 (100)	35 (100)	121 (100)

Factors associated with increasing severity of EPVS

After comparing the three severity categories of EPVS in the CSO and BG for clinical and radiological risk factors associated with increasing severity (all the variables shown in Table 1), smoking history (p=0.05), non-CAA related ICH (p=0.001) and mean WMC score (p<0.00001) (Supplementary Figure 1) were significantly associated with increasing severity of BG EPVS; only increasing mean age was significantly associated with increasing severity of CSO EPVS (p=0.03) (data not shown).



Supplementary Figure 1. Box and whisker plots illustrating white matter changes (WMC) score distributions according to enlarged perivascular spaces (EPVS) severity category in the basal ganglia. Comparisons were performed using ANOVA.

Supplementary Table 3. Univariable (unadjusted) ordinal logistic regression analysis showing predictors of increased total EPVS severity in the whole cohort.

	Total EPVS	
	OR (95% CI)	**P-Value**
Age (per 10 years older)	**1.43 (1.07-1.92)**	**0.016**
Sex, male	0.56 (0.29-1.08)	0.083
History of hypertension (Yes vs. No)	0.67 (0.32-1.39)	0.280
History of smoking (Yes vs. No)	**2.24 (1.09-4.62)**	**0.028**
Diabetes (Yes vs. No)	0.94 (0.38-2.29)	0.888
On statins (Yes vs. No)	0.80 (0.36-1.79)	0.593
On antithrombotics (Yes vs. No)	0.65 (0.32-1.32)	0.231
First ever ICH, n yes (%)	0.83 (0.41-1.67)	0.595
CAA-related ICH (Yes vs. No)	0.75 (0.38-1.47)	0.398
Lacunar infarct (Yes vs. No)	2.79 (0.99-7.84)	0.052
Multiple ICHs (Yes vs. No)	0.94 (0.48-1.82)	0.847
CMBs presence (Yes vs. No)	1.92 (0.92-3.99)	0.081
Strictly lobar CMBs (Yes vs. No)	1.26 (0.65-2.44)	0.496
Lobar CMBs (Yes vs. No)	1.86 (0.91-3.81)	0.091
Deep CMBs (Yes vs. No)	1.43 (0.68-3.03)	0.348
Mean total WMC score (for each unit increase)	**1.10 (1.03-1.18)**	**0.003**

Predictors of total EPVS severity in the whole cohort

In univariable ordinal logistic regression analysis, significant predictors of increasing total EPVS severity were age, smoking and mean WMC score (Supplementary Table 2). Gender, presence of lacunar infarct and presence of CMBs had a marginal effect (Supplementary Table 3). In an adjusted model including presence of lacunes, lobar and deep CMBs, age (OR: 1.38, per 10 years increase; 95%CI: 1.02-1.87; p=0.036) and WMC (OR: 1.12; 95%CI: 1.04-1.20; p=0.002) were still independent predictors of severe total EPVS (Supplementary Table 4).

Supplementary Table 4. Multivariable (adjusted) ordinal logistic regression analysis showing predictors of increased total EPVS severity in the whole cohort.

	Total EPVS	
	OR (95%CI)	**P-Value**
Age (per 10 years older)	**1.38 (1.02-1.87)**	**0.036**
Lobar microbleeds (Yes vs. No)	2.63 (0.28-25.15)	0.401
Deep microbleeds (Yes vs. No)	1.75 (0.21-14.76)	0.609
Mean total WMC score (for each unit increase)	**1.12 (1.04-1.20)**	**0.002**
Lacunar infarct (Yes vs. No)	1.00 (0.99-1.01)	0.913