Supplementary Table 1 Presence or absence of the association between cerebral amyloid angiopathy and microinfarcts

Reference	Subjects	CAA classification	Microinfarct	Macro or micro-infarcts	GM and WM	Correlation between CAA severity and cortical (micro)infarcts
Olichney JM, et al. 1995	145AD cases	0, none; 1, scattered; 2, some; 3, widespread circumferential; 4, severe with vessel morphological changes (Thioflavin S)	Number of cases with infarcts	Combined	Combined	The presence of severe CAA was associated with cerebral infarctions with an odds ratio of 3.5 (95% CI 1.4–8.9) compared with mild CAA.
Ellis RJ, et al. 1996	117 AD cases	0, none; 1, sparse or mild; 2, moderate; 3, frequent or severe (Congo red, Thioflavin S, or Aβ)	Number of cases with microinfarcts	Microinfarcts	Combined	12 cases with microinfarcts only (no haemorrhage or gross infarct), No association
Haglund M, et al. 2004	22 cases (11 AD; 11 VaD-ae)	The extent and the severity were assessed. The severity was graded on a scale from 1-3 (Goulding JM, 1999) (Aβ)	Cortical infarcts, Number (H&E)	Combined	Cortex	Significant correlation between the proportion of amyloid-positive vessels in the cortex and the amount of cortical infarcts (p=0.018, r=0.5)
Haglund M, et al. 2006.	26 VaD cases	% (affected/total vessels) (Aβ)	Cortical microinfarct, Number (H&E)	Microinfarcts	Cortex	Association between meningeal CAA and cortical microinfarcts (temporal, p = 0.002, r = 0.59; parietal, p = 0.008, r = 0.51).
Launer LJ, et al. 2008	439 men (99% had AD pathology, HAAS)	absent or present (Aβ)	Number of cases with microinfarcts	Microinfarcts	Combined	No association Odds ratio, 1.03 (0.53-2.0)
Soontornniyomkij V, et al. 2010	39 AD cases (28 definite, 9 probable, 2 possible)	mild I vs. severe III (Vonsattel)	Microinfarct, Number (CD68)	Microinfarcts	Combined	Significant difference in the number of microinfarcts between severe and mild CAA cases (p=0.008; two-tailed Mann-Whitney test)
This study by Okamoto Y, et al.	31 cases (14 AD and 17 non-AD)	mild I vs. moderate II or severe III (Vonsattel) (Congo Red, Aβ)	Cortical microinfarct, Number (H&E)	Microinfarcts	Cortex	Significant association between CMI density and CAA severity (multivariate analysis, p = 0.0022).

Abbreviations; CAA, cerebral amyloid angiopathy; GM, gray matter; HAAS, Honolulu-Asia Aging Study; VaD, vascular dementia; VaD-ae, vascular dementia with additional mild Alzheimer encephalopathy (Alzheimer pathology that does not fulfill criteria for AD); WM, white matter

Supplementary Table 2 Clinical and pathological diagnosis of the subjects

Case No.	Clinical diagnosis	Cause of death	Vascular risk factors	Postmortem delay (hr)	Fixation time (days)	Neuropathological diagnosis	Other neuropathological findings	Comorbidity
1	AD	ND	DM	2.5	17	AD	A petechiae in the right internal capsule, A lacunar in the left putamen	—
2	AD brain tumor	Brain tumor	HT	2.5	26	AD	A lacunar in the left globus pallidus	Well-differentiated adenocarcinoma
3	Airway obstruction	Asphyxia	Af Valvular replacement	2.0	19	AD	An old infarct (3 x 5 mm) in the right cerebellum	Respirator support for 4 months
4	AD Asphyxia	Asphyxia	—	11.0	70	AD	—	—
5	Dementia	ND	ND	ND	ND	AD	—	Respirator support for 7 days
6	AD Asphyxia	Debilitation	—	4.0	7	AD	—	—
7	Dementia	Asphyxia	ND	3.5	13	AD	An old infarct in the putamen	ND
8	AD Stomach cancer	Pneumonia	ND	17.5	7	AD	Multiple lacunas	Stomach cancer, liver metastasis
9	AD Pneumonia	Pneumonia	HT	7.0	6	AD	An old infarct in the right putamen	ND
10	Dementia	Peritonitis	—	10.5	330	AD	—	OMI
11	ND	ND	ND	ND	ND	AD	—	ND

12	Dementia Pneumonia	Pneumonia	—	18.5	32	AD	—	—
13	AD	Lobar hemorrhage	—	13.5	19	AD	An old hemorrhage (5 x 2 mm) in the left cerebellum	OMI
14	Lobar hemorrhage Stomach cancer	Stomach cancer	Af	15.5	21	AD	—	—
15	Dementia Old cerebral infarct CAD	Pneumonia	—	44.5	31	SIVD	Multiple lacuna in the basal ganglia and thalamus	OMI
16	Pancreas cancer DIC	Pancreas cancer	DM	13.0	30	Only mild senile changes	—	—
17	Dementia	Pneumonia	—	1.5	15	Only mild senile changes	An old small infarct in the left cerebellum	Mitral vegetation
18	Multiple infarcts Pneumonia	CHF, pneumonia	SSS, Pacemaker	17.5	23	Only mild senile changes	Macroinfarcts in the frontal and temporoparietal lobes	—
19	PD Pneumonia	Colon cancer, Sepsis	—	26.5	23	PD	An old infarct in the left cerebellum	—
20	ALS	Respiratory failure	HT, DM	15.5	18	ALS	—	Cardiomegaly
21	Dementia	Debilitation	DM	2.5	36	SIVD	Two lacunas in the right thalamus and the left caudate head	OMI
22	CHF heart valvular disease	CHF, pneumonia	Valvular disease	27.5	17	Only mild senile changes	—	Combined valvular disease, AAA 3*3.5 cm
23	DLB	Pneumonia	—	45.5	49	DLBD	—	—
24	Parkinsonism and	Ileus	—	2.5	22	PSP	Multiple lacunas in the right	—

	dementia						caudate head and putamen	
25	Thalamic hemorrhage with ventricular rupture	Thalamic hemorrhage	HT	1.5	29	Thalamic hemorrhage	Multiple lacunas in the right putamen, white matter and pontine base	OMI, LC type C
26	Parkinsonism and dementia	Pneumonia	Severe orthostatic hypotension	15.5	46	PD	An old infarct in left parietal white matter	OMI
27	ALS	Respiratory failure	—	16.0	26	ALS	—	—
28	Cerebral infarct Top of basilar syndrome	Cerebral infarct	Af, Pacemaker	22.5	61	Cerebral infarct	Occluded basillar artery	—
29	Dementia	Hyponatremia	Infectious endocarditis	2.5	23	CBD	Chronic subdural hematoma, Multiple lacunas in the putamen and pons	—
30	Lobar hemorrhage	Lobar hemorrhage	HT	10.0	11	Lobar hemorrhage	—	—
31 [1]	PACNS	PACNS	HT	2.5	33	CAA-related inflammation	—	—

Abbreviation: AAA, aortic aorta aneurysm; AD, Alzheimer's disease; Af, atrial fibrillation; ALS, amyotrophic lateral sclerosis; CAD, coronary artery disease; CHF, congestive heart failure; DIC, disseminated intravascular coagulation; DLB, Dementia with Lewy bodies; DLBD, diffuse Lewy body disease; DM, diabetes mellitus; HT, hypertension; LC, liver cirrhosis; OMI, old myocardial infarction; PACNS, primary angiitis of the central nervous system; PD, Parkinson's disease; PSP, progressive supranuclear palsy; SIVD, subcortical ischemic vascular dementia; SSS, sick sinus syndrome; ND, not determined.

Supplementary Table 3 Frequency of microvascular complications in the three animal cohorts

BCAS-operated Tg-SwDI mouse							Sham-operated Tg-SwDI mouse						
		Number of microinfarcts							Number of microinfarcts				
		Distance from the midline (mm)							Distance from the midline (mm)				
Age (week)	No.	+1	+2	+3	+4	total	Age (week)	No.	+1	+2	+3	+4	total
18	1	0	0	0	0	0	18	1	0	0	0	0	0
	2	1	2	3	4	10		2	0	0	0	0	0
	3	0	0	0	0	0		3	0	0	0	0	0
	4	0	0	0	0	0		4	0	0	0	0	0
	5	0	0	1	0	1							
	6	0	0	1	0	1							
24	1	1	4	2	1	8	24	1	0	0	0	0	0
	2	1	0	0	0	1		2	0	0	0	0	0
	3	0	0	0	0	0		3	0	0	0	0	0
	4	0	0	0	0	0		4	0	0	0	0	0
	5	0	0	0	0	0		5	0	0	0	0	0
	6	0	0	1	0	1		6	0	0	0	0	0
	7	0	0	0	0	0							
32	1	0	0	0	0	0	32	1	0	0	0	0	0
	2	0	0	0	0	0		2	0	0	0	0	0
	3	0	0	0	0	0		3	0	0	0	0	0
	4	1*	1	0	1	3		4	0	0	0	0	0

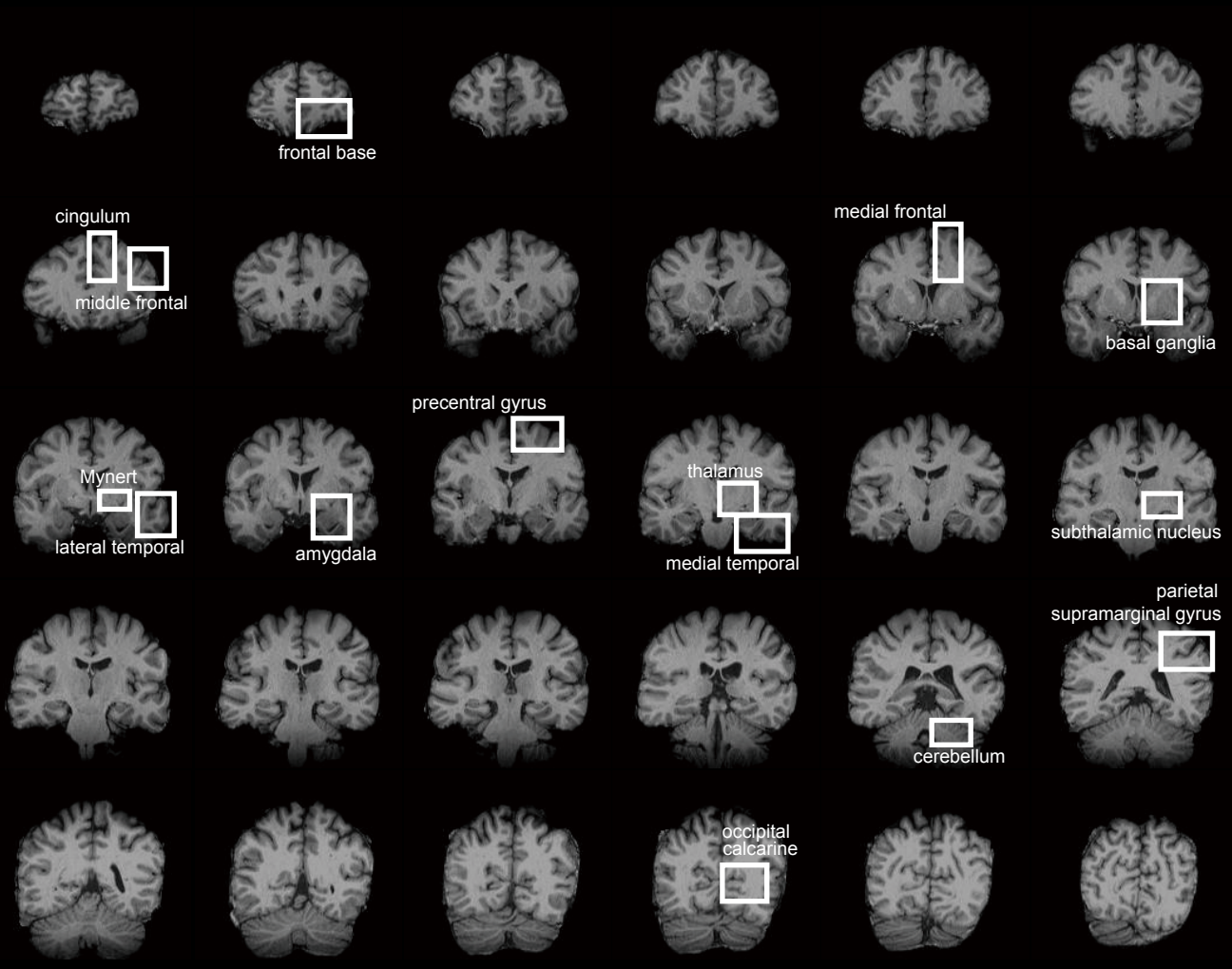
* Two microhaemorrhagic foci were present in addition to a microinfarct.

BCAS, bilateral common carotid artery stenosis; Tg-SwDI mouse, a transgenic mouse that expresses human vasculotropic Swedish/Dutch/Iowa mutant amyloid precursor protein

Supplementary Reference

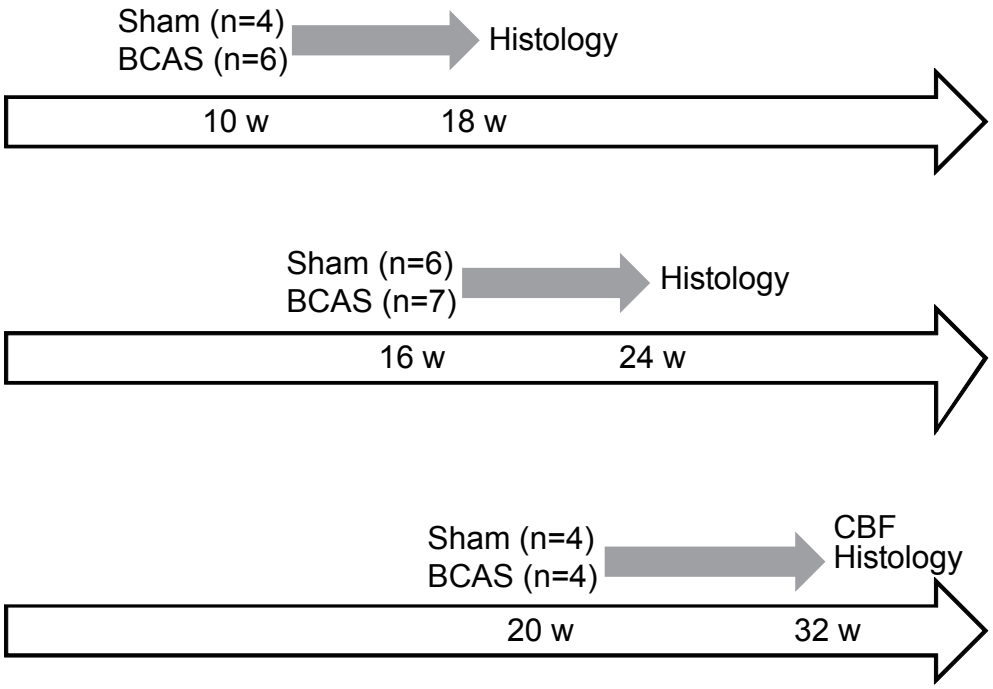
1. Takeda A, Tatsumi S, Yamashita M, Yamamoto T (2007) Granulomatous angiitis of the CNS associated with cerebral amyloid angiopathy--an autopsied case with widespread involvement. Brain Nerve 59: 537-543

Supplementary Fig. 1



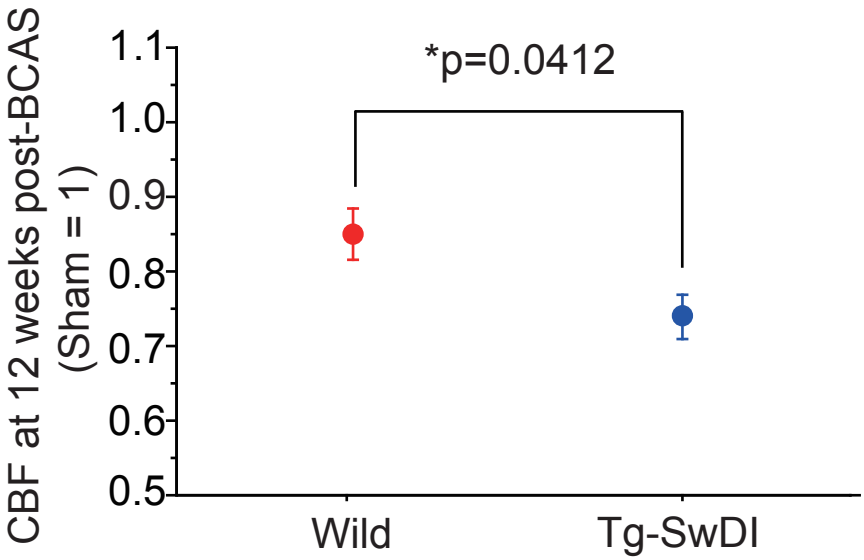
MRI atlas with 1 cm slice interval showing the location of sampled brain sections.

Supplementary Fig. 2



Experimental protocol of the current animal study. Tg-SwDI mice at 10, 16, and 20 weeks of age were subjected to sham or BCAS operation and underwent histological evaluation at 18, 24, and 32 weeks of age, respectively. In the third cohort, CBF was also recorded at 32 weeks of age.

Supplementary Fig. 3



CBF of wild-type and Tg-SwDI mice after BCAS operation. BCAS operation in 20 week-old wild-type mice reduced CBF by 15% after 12 weeks while in Tg-SwDI mice the CBF reduction was 26%, indicating accelerated vascular compromise due to Aβ deposition in Tg-SwDI mice (p=0.0412). In both genotypes, the baseline value of CBF in the sham-operated mice was set at 1.0.