Supplemental Materials

(I) Cohort Characteristics

Characteristics	ROS (n=718)	MAP (n=746)	MARS (n=25)	*p*-value
Demographics, Mean (SD) or n (%)				
Age at death	88.12 (6.98)	89.89 (6.29)	82.70 (9.62)	<0.001
Education	18.10 (3.45)	14.51 (2.89)	14.13	<0.001
Sex, Women	464 (64.6%)	520 (69.7%)	18 (72.0%)	0.06
Neuropathology, Mean (SD) or N (%)				
Pathologic Diagnosis of AD	455 (63.4%)	490 (65.7)	12 (48.0%)	0.31
β-Amyloid burden	1.42 (1.04)	1.76 (1.20)	1.35	<0.001
Tau Tangles burden	1.54 (1.30)	1.68 (1.35)	1.69	0.14
Arteriolosclerosis (moderate – severe)	226 (31.5%)	271 (36.3%)	7 (28.0%)	0.18
CAA (moderate – severe)	254 (36.7%)*	261 (35.2%)*	3 (12.0%)	0.06
Atherosclerosis (moderate – severe)	272 (38.2%)*	231 (31.01%)	1 (4.0%)	<0.001
Cortical Microinfarcts	114 (15.9%)	136 (18.2%)	4 (16.0%)	0.49
Subcortical Microinfarcts	113 (15.7%)	103 (13.8%)	2 (8.0%)	0.45

*Indicates data missing

(II) Assessment for neuritic plaque pathology

For assessment of neuritic plaque burden, manual counts using a 1 mm^2 area grid were obtained by experienced neuropathologists on Bielschowsky silver stain from 4 regions; midfrontal, mid temporal, entorhinal, and inferior partial cortices. For analyses each regional count for neuritic plaques was scaled by dividing by the corresponding standard deviation. Scaled regional measures were averaged to obtain a summary measure for neuritic plaque burden, and used for analyses.

(III) Inter-rater protocol for PHF-tau neurofibrillary tangle burden

Standard protocols are followed in which new raters assess 50-100 slides, representative of a range of pathology, that have already been rated by an experienced rater. A percentage of variation in the square-root transformed value of tangles due to rater within slides is obtained. For neurofibrillary tangles, the variability in the data within slide due to rater is less than 5%.

(IV) Assessment for subcortical frontal and parietal white matter arteriolosclerosis

In a subset of participants (n=749), we have assessed vessels for arteriolosclerosis pathology in both subcortical frontal white matter and subcortical parietal white matter, blind to all other neuropathologic and clinical data. We find a weak positive correlation between arteriolosclerosis pathology in the basal ganglia with both subcortical frontal ($Rs = 0.2$, $p<0.001$) and subcortical parietal white matter ($Rs = 0.2$, $p<0.001$). Persons with arteriolosclerosis pathology in both basal ganglia and subcortical white matter was common. 50% of persons with any level of arteriolosclerosis pathology (mild/moderate/severe) was present in both the basal ganglia and subcortical frontal white matter, and 42% in both basal ganglia and subcortical partial white matter. These data suggest that our assessment of arteriolosclerosis in the basal ganglia is moderately representative of arteriolosclerosis in other regions that are closely connected to frontal and parietal lobes.

(V) Interaction of cerebral vessel pathology with neuritic plaque burden in relation to probability of microinfarct burden

Model Set	Predictors	Interaction	Cortical microinfarcts	Subcortical microinfarcts
1	**Arteriolosclerosis**		0.04 (0.11, 0.73)	0.29 (0.12,0.02)
	Neuritic plaque		-0.26 (0.15, 0.09)	-0.05 (0.17,0.77)
		Arteriolosclerosis x Neuritic plaque	0.12 (0.09, 0.15)	0.03 (0.10,0.76)
2	**CAA**		0.01 (0.11,0.96)	0.08 (0.12,0.52)
	Neuritic plaque		-0.40 (0.17, 0.02)	0.12 (0.17,0.48)
		CAA x Neuritic plaque	**0.21 (0.09,0.02)**	-0.11 (0.10,0.30)

Log-odds ratio estimates were derived from logistic regression models in which cortical or subcortical microinfarct burden was the outcome. Models included an interaction term between vessel pathologies, either CAA or arteriolosclerosis with neuritic plaque burden. All model sets were adjusted for age, sex, education, atherosclerosis, and tangle burden. In addition, model set 1 was further adjusted for CAA, and model set 2 was further adjusted for arteriolosclerosis. Cell value represents log-odds estimate (SE, p-value)

(VI) Sensitivity Analyses

In sensitivity analyses, we fit the same interaction models but excluded persons with tangle burden in the 90th – 100th. In these models, tau pathology was not associated with cortical microinfarcts in the absence of arteriolosclerosis (estimate = -0.18; SE=0.18; p=0.31) or CAA pathology (estimate = -0.25; SE=0.15; p=0.11). Additionally, in separate models we examined the association of tau tangles with cortical microinfarcts in a subset of older persons where arteriolosclerosis or CAA pathology severity was graded as none. Similarly, tau pathology was not associated with cortical microinfarcts [(estimate = -0.09; SE=0.13; p=0.50) and (estimate = -0.05; SE = 0.23; p=0.81), respectively].