

Supplementary Table 1. Odds of being cognitively resilient to intermediate or high AD pathology versus not using inverse probability weights to account for selection bias into the autopsy sample*

	Inverse probability weighted demographic and non-AD neuropathology adjusted OR (95%CI)
College degree	
Yes	2.13 (1.04-4.35)
CERAD	
Frequent	0.75 (0.36-1.55)
Braak	
IV	0.41 (0.11-1.47)
V	0.28 (0.09-0.89)
VI	0.07 (0.02-0.23)
Cortical or deep microinfarcts	
2+	0.38 (0.15-0.95)
Hippocampal sclerosis	
Yes	0.20 (0.06-0.67)
Lewy bodies in isocortex	
Yes	0.28 (0.07-1.03)
Brain weight (per gm)	1.004 (1.001-1.007)

*Inverse probability weights generated from a selection model predicting the probability of being autopsied among those that died based on age at death, age at baseline, dementia status, gender, education, race, and ACT cohort

Supplementary table 2. Baseline characteristics of people with and without cognitive resilience to AD pathology; sensitivity analysis limiting cognitive resilience group to people with CASI scores ≥ 86 within one year before death

	Intermediate or high AD pathology		
	Not resilient	Cognitively Resilient	p-value
	N (%‡)	N (%‡)	(chi2)
	N=208*	N=32†	
ACT cohort:			0.08
Original	139 (66.8)	59 (81.3)	
Expansion	49 (23.6)	2 (6.3)	
Replacement	20 (9.6)	4 (12.5)	
Baseline median age (IQR)	77 (73-82)	78 (73-85)	0.88
Median years between baseline and death (IQR)	13 (9-16)	9 (6-14)	0.09
Sex:			
Male	75 (36.1)	10 (31.5)	0.60
Female	133 (63.9)	22 (68.8)	
Median years of education (IQR)	14 (12-16)	15 (12-17)	0.36
College degree:			
No	141 (67.8)	17 (53.1)	0.10
Yes	67 (32.2)	15 (46.9)	
Race:			
Non-Hispanic white	196 (94.2)	31 (96.9)	0.54
Non-white	12 (5.8)	1 (3.1)	
Hypertension	71 (34.5)	11 (34.4)	0.99
Diabetes	19 (9.1)	2 (6.3)	0.59

Stroke	4 (1.9)	1 (3.1)	0.66
Cerebrovascular disease	19 (9.2)	3 (9.4)	0.98
Coronary heart disease	32 (15.5)	3 (9.4)	0.37
Congestive heart failure	2 (1.0)	0 (0)	0.58
Smoking:			
Never	113 (54.3)	14 (43.8)	0.52
Past	86 (41.4)	16 (50.0)	
Current	9 (4.3)	2 (6.3)	
BMI (kg/m ²)			
<25	84 (41.0)	13 (41.9)	0.89
25-29.9	81 (39.5)	11 (35.5)	
30+	40 (19.5)	7 (22.6)	
Median head circumference cm (IQR)	56.2 (55.0-58.0)	56.3 (55.2-57.9)	0.80
Regular exercise (≥ 15 min 3x week)	151 (73.0)	25 (78.1)	0.54
Number of difficult activities of daily living			
0	159 (76.8)	23 (71.9)	0.77
1	29 (14.0)	6 (18.8)	
2+	19 (9.2)	3 (9.4)	
APOE $\epsilon 4$ allele	79 (39.3)	10 (31.3)	0.38

*People diagnosed with dementia before death, and a CERAD score of intermediate or frequent AND a BRAAK stage of III-VI

**People diagnosed with dementia before death, and a CERAD score of frequent AND a BRAAK stage of V-VI

†People with a CASI score ≥ 86 within 1 year of death and no dementia diagnosis, and a CERAD score of intermediate or frequent AND a BRAAK stage of III-VI

‡Percent calculated among people with non-missing covariate data.

Supplementary table 3. Neuropathology characteristics of people with and without cognitive resilience to AD pathology; sensitivity analysis limiting resilience group to people with CASI scores ≥ 86 within one year before death

	Intermediate or high AD pathology		
	Not resilient	Cognitively Resilient	p-value
	N (%‡)	N (%‡)	(chi2)
	N=208*	N=32†	
Median age at death (IQR)	91 (88-95)	89 (85-93)	0.26
Median years between dementia diagnosis and death (IQR)	5.2 (3.2-7.5)	N/A	N/A
Median years between last CASI score ≥ 86 and death (IQR)	N/A	0.5 (0.2-0.6)	N/A
CERAD			
Intermediate	75 (36.1)	18 (56.3)	0.03
Frequent	133 (64.0)	14 (43.8)	
Braak			
III	17 (8.2)	15 (46.9)	<0.001
IV	27 (13.0)	3 (9.4)	
V	76 (36.5)	8 (25.0)	
VI	88 (42.3)	6 (18.8)	
Atherosclerosis			
None/mild	45 (21.7)	11 (35.5)	0.09
Moderate/severe	162 (78.3)	20 (64.5)	
Arteriolosclerosis			
None/mild	28 (15.3)	3 (13.6)	0.84
Moderate/severe	155 (84.7)	19 (86.4)	

Macroscopic cystic infarcts			
None	84 (56.0)	19 (82.6)	0.02
Any	66 (44.0)	4 (17.4)	
Cortical or deep microinfarcts			
0-1	135 (64.9)	28 (87.5)	0.01
2+	73 (35.1)	4 (12.5)	
Hippocampal sclerosis			
No	157 (77.0)	30 (96.8)	0.01
Yes	47 (23.0)	1 (3.2)	
Amyloid angiopathy			
None/mild	152 (73.8)	26 (81.3)	0.37
Moderate/severe	54 (26.2)	6 (18.8)	
Lewy bodies in isocortex			
No	184 (89.8)	30 (96.8)	0.32
Yes	21 (10.2)	1 (3.2)	
Brain weight mean, gm (SD)	1165 (136)	1244 (153)	0.004

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†People with a CASI score ≥ 86 within 1 year of death and no dementia diagnosis, and a CERAD score of intermediate or frequent AND a BRAAK stage of III-VI

‡Percent calculated among people with non-missing neuropathology data.

Supplementary table 4. Odds of being cognitively resilient versus not (defined by intermediate or high AD pathology) adjusted for demographic characteristics and non-AD neuropathology findings; sensitivity analysis limiting cognitive resilience group to people with CASI scores ≥ 86 within one year before death

	Demographic- adjusted*		Demographic and non- AD neuropathology	
	OR (95% CI)	p-value	adjusted** OR (95% CI)	p-value
College degree				
No	1.0		1.0	
Yes	1.87 (0.87-4.04)	0.11	1.74 (0.67-4.50)	0.25
CERAD				
Intermediate	1.0		1.0	
Frequent	0.49 (0.22-1.07)	0.07	0.91 (0.32-2.60)	0.87
Braak				
III	1.0		1.0	
IV	0.16 (0.04-0.67)	0.01	0.23 (0.04-1.19)	0.08
V	0.15 (0.05-0.43)	<0.001	0.28 (0.08-0.98)	0.047
VI	0.09 (0.03-0.28)	<0.001	0.13 (0.03-0.50)	0.003
Cortical or deep microinfarcts				
0-1	1.0		1.0	
2+	0.28 (0.09-0.84)	0.02	0.23 (0.06-0.90)	0.04
Hippocampal sclerosis				
No	1.0		1.0	
Yes	0.13 (0.02-0.99)	0.049	0.17 (0.02-1.40)	0.10
Lewy bodies in isocortex				
No	1.0		1.0	
Yes	0.25 (0.03-2.00)	0.19	0.23 (0.02, 2.30)	0.21
Brain weight (per gm)	1.003 (1.001-1.006)	0.02	1.005 (1.001, 1.009)	0.01

* adjusted for age at baseline, age at death, and college degree.

** adjusted for age at baseline, age at death, college degree, CERAD, Braak, microinfarcts, hippocampal sclerosis, Lewy body disease, and brain weight. Model includes 223 observations with non-missing data.

Supplementary table 5. Baseline characteristics of people with and without cognitive resilience to AD pathology; sensitivity analysis limiting to people who lived to at least age 85

	Intermediate or high AD pathology		
	Not resilient	Cognitively Resilient	p-value
	N (%‡)	N (%‡)	(chi2)
	N=181*	N=50†	
ACT cohort:			
Original	124 (68.5)	35 (70.0)	0.25
Expansion	43 (23.8)	8 (16.0)	
Replacement	14 (7.7)	7 (14.0)	
Baseline median age (IQR)	78 (74-83)	82 (73-85)	0.44
Median years between baseline and death (IQR)	13 (10-17)	13 (7-16)	0.55
Sex:			
Male	59 (32.6)	19 (38.0)	0.48
Female	122 (67.4)	31 (62.0)	
Median years of education (IQR)	14 (12-16)	15 (12-17)	0.35
College degree:			
No	121 (66.9)	26 (52.0)	0.05
Yes	60 (33.2)	24 (48.0)	
Race:			
Non-Hispanic white	170 (93.9)	45 (90.0)	0.33
Non-white	11 (6.1)	5 (10.0)	
Hypertension	60 (33.5)	16 (32.7)	0.91
Diabetes	14 (7.7)	3 (6.1)	1.0
Stroke	4 (2.2)	2 (4.0)	0.61

Cerebrovascular disease	14 (7.8)	5 (10.0)	0.61
Coronary heart disease	25 (13.9)	6 (12.0)	0.73
Congestive heart failure	1 (0.6)	1 (2.0)	0.38
Smoking:			
Never	101 (55.8)	25 (50.0)	0.73
Past	72 (39.8)	23 (46.0)	
Current	8 (4.4)	2 (4.0)	
BMI (kg/m ²)			
<25	75 (42.1)	19 (40.4)	0.88
25-29.9	69 (38.8)	20 (42.6)	
30+	34 (19.1)	8 (17.0)	
Median head circumference cm (IQR)	56.0 (55.0-57.8)	56.6 (55.2-58.3)	
Regular exercise (≥ 15 min 3x week)	133 (73.9)	39 (78.0)	0.55
Number of difficult activities of daily living			
0	137 (76.1)	37 (74.0)	0.86
1	27 (15.0)	9 (18.0)	
2+	16 (8.9)	4 (8.0)	
APOE $\epsilon 4$ allele	64 (36.4)	18 (36.7)	0.96

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†People with a CASI score ≥ 86 within 2 years of death and no dementia diagnosis, and a CERAD score of intermediate or frequent AND a BRAAK stage of III-VI

‡Percent calculated among people with non-missing covariate data.

Supplementary table 6. Neuropathology characteristics of people with and without cognitive resilience to AD pathology; sensitivity analysis limiting to people who lived to at least age 85

	Intermediate or high AD pathology		
	Not resilient	Cognitively Resilient	p-value
	N (%‡)	N (%‡)	(chi2)
	N=181*	N=50†	
Median age at death (IQR)	92 (89-96)	92 (88-96)	0.97
Median years between dementia diagnosis and death (IQR)	5.3 (3.3-7.6)		
		N/A	N/A
Median years between last CASI score \geq 86 and death (IQR)	N/A	1.2 (0.5-1.6)	N/A
CERAD			
Intermediate	66 (36.5)	25 (50.0)	0.08
Frequent	115 (63.5)	25 (50.0)	
Braak			
III	16 (8.8)	14 (28.0)	<0.001
IV	25 (13.8)	8 (16.0)	
V	68 (37.6)	21 (42.0)	
VI	72 (39.8)	7 (14.0)	
Atherosclerosis			
None/mild	35 (19.3)	9 (18.4)	0.88
Moderate/severe	146 (80.7)	40 (81.6)	
Arteriolosclerosis			
None/mild	24 (14.8)	9 (21.4)	0.30
Moderate/severe	138 (85.2)	33 (78.6)	

Macroscopic cystic infarcts			
None	73 (57.0)	23 (71.9)	0.13
Any	55 (43.0)	9 (28.1)	
Cortical or deep microinfarcts			
0-1	114 (63.0)	41 (82.0)	0.01
2+	67 (37.0)	9 (18.0)	
Hippocampal sclerosis			
No	135 (75.4)	45 (91.8)	0.01
Yes	44 (24.6)	4 (8.2)	
Amyloid angiopathy			
None/mild	131 (73.2)	35 (70.0)	0.66
Moderate/severe	48 (26.8)	15 (30.0)	
Lewy bodies in isocortex			
No	160 (89.9)	47 (95.9)	0.26
Yes	18 (10.1)	2 (4.1)	
Brain weight mean, gm (SD)	1194 (133)	1219 (142)	0.01

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‡Percent calculated among people with non-missing neuropathology data.