

# Supplementary Material A

Supplementary Table 1: Characteristics of individuals in the Manchester cohort

Code	Sex	Age at death	Clinical diagnosis	Braak stage (AD)	APOE Status	Post-Mortem Delay (hours)	Whole-brain weight (g)	Brain pH	Cause of Death
AD1	M	88	Alzheimer's Disease	V	3/4	75	1027	NA	NA
AD2	M	69	Alzheimer's disease	VI	3/3	96	1160†	NA	NA
AD3	M	65	Alzheimer's disease	VI	3/3	72*	NA	NA	NA
AD4	F	61	Alzheimer's disease	VI	3/4	130	1120	NA	NA
AD5	F	89	Alzheimer's disease	V-VI	3/3	72	NA	NA	NA
AD6	M	76	Alzheimer's disease	V-VI	3/4	96*	1359	NA	NA
AD7	M	83	Alzheimer's disease	IV-V	3/3	96	1046†	NA	NA
AD8	F	88	Alzheimer's disease	VI	3/3	72	900†	NA	NA

AD9	M	87	Alzheimer's disease	IV	3/4	49	1066	NA	NA
C1	F	92	No dementia or brain disease	II	3/4	37	1080 <sup>†</sup>	NA	Myocardial infarction
C2	F	87	No dementia or brain disease	I-II	3/3	39	1160 <sup>†</sup>	NA	Anteroseptal myocardial infarction; coronary atherosclerosis; left ventricular hypertrophy
C3	M	89	No dementia or brain disease	II	3/3	27	1400 <sup>†</sup>	NA	Multi-organ failure, septicaemia, cellulitis, heart failure
C4	M	95	No dementia or brain disease	I-II	3/3	12	1200 <sup>†</sup>	NA	Prostatic carcinoma
C5	F	87	No dementia or brain disease	0-I	3/4	24	1152	NA	Cardiac failure, COPD, renal impairment, osteoarthritis
C6	M	84	No dementia or brain	I	3/3	69.5	1494	5.84	NA

			disease						
C7	F	90	No dementia or brain disease	0-I	3/3	39	1050	NA	Frailty of old age
C8	F	82	No dementia or brain disease	0-I	3/3	61	1020†	NA	Metastatic ovarian cancer
C9	F	94	No dementia or brain disease	I-II	3/3	70	1276	5.87	Carcinoma of the appendix

\*Estimated PMD (provided by the Manchester Brain Bank); †brain weighed at point of fixation by brain bank. Abbreviation: NA, not available

Supplementary Table 2: Characteristics of individuals in the Auckland cohort

Code	Sex	Age at death	Clinical diagnosis	Braak stage (AD)	APOE Status	Post-Mortem Delay (hours)	Whole-brain weight (g)	Brain pH	Cause of Death
AD19	M	60	Alzheimer's Disease	6	NA	7.0	1020	7.0	Alzheimer's disease
AD20	F	62	Alzheimer's disease	6	NA	6.0	831	6.0	Alzheimer's disease
AD21	F	63	Alzheimer's disease	6	NA	7.0	1080	7.0	Bronchopneumonia
AD22	F	70	Alzheimer's disease	5	NA	7.0	1044	7.0	Lung cancer
AD23	M	73	Alzheimer's disease	4	NA	4.0	1287	4.0	GI haemorrhage
AD24	F	74	Alzheimer's disease	5	NA	8.5	1062	8.5	Metastatic cancer
AD25	M	74	Alzheimer's disease	6	NA	12.0	1355	12.0	Pseudomonas bacteraemia
AD26	M	77	Alzheimer's disease	6	NA	4.5	1180	4.5	Myocardial infarction
AD27	M	80	Alzheimer's disease	5	NA	5.5	1039	5.5	Bronchopneumonia/ pulmonary oedema

C19	M	61	No dementia or brain disease	0	NA	7.0	1258	7.0	Ischaemic heart disease
C20	F	64	No dementia or brain disease	0	NA	5.5	1260	5.5	Pulmonary embolism
C21	F	63	No dementia or brain disease	0	NA	12.0	1280	12.0	Ruptured aorta
C22	F	72	No dementia or brain disease	0	NA	9.0	1230	9.0	Emphysema
C23	M	66	No dementia or brain disease	0	NA	9.0	1461	9.0	Ischaemic heart disease
C24	F	76	No dementia or brain disease	2	NA	12.0	1094	12.0	Metastatic carcinoma
C25	M	73	No dementia or brain disease	0	NA	13.0	1315	13.0	Ischaemic heart disease
C26	M	78	No dementia or brain disease	0	NA	7.5	1260	7.5	Ruptured aortic aneurysm
C27	M	78	No dementia or brain disease	0	NA	12.0	1416	12.0	Ruptured MI

Abbreviation: NA = Not available

Supplementary Table 3: PMD, Braak stage and age of all brains listed in databases of the Manchester brain bank

Variable		Manchester Samples	
PMD†		82 (4-279) <sup>1</sup>	
Braak Stage	0	I/II	P-Value
Age†	68 (44-90)	85 (55-103)	1.4x10 <sup>-6</sup> ****

Values are mean (range). † Data taken from all individuals in database, irrespective of diagnosis. <sup>1</sup>Data obtained from MRC Brain Bank database on 07/06/2019 from 420 cases with available PMD data; data unavailable for 20 individuals. \*\*\*\* p < 0.0001

Supplementary Table 4: Characteristics of Manchester experimental cohort

Variable	Controls	AD Cases
Number	9	9
Age	89 (82-95)	83 (61-89)*
Male Sex, n (%)	6 (66.7)	3 (33.3)
Braak Stage	I-II	IV-V****
PMD (hours)	75 (49 – 130)	39 (12 – 70)***
Whole-brain weight (g) †	1160 (1020 – 1494)	1066 (900 – 1359)

Values are: age, PMD, Braak stage, and whole-brain weight median (range); \*  $p < 0.05$ , \*\*\*  $p < 0.001$ , \*\*\*\*  $p < 0.0001$ . †

Whole-brain weights were unavailable for two AD cases.

Supplementary Table 5: Characteristics of Auckland experimental cohort

Variable	Controls	AD Cases
Number	9	9
Age	72 (61 - 78)	73 (60 - 80)
Male Sex, n (%)	5 (55.6)	5 (55.6)
Braak Stage	0 (0 - II)****	VI (IV - VI)
PMD (hours)	9 (7 - 13)*	7 (4 - 12)
Whole-brain weight (g) †	1062 (831 - 1355)	1260 (1094 - 1461)
Brain pH	7.0 (4.0 - 12)*	9.0 (5.5 - 13.0)

Values are: age, PMD, Braak stage, pH, and whole brain weight median (range); \*  $p < 0.05$ , \*\*\*\*  $p < 0.0001$ .

Abbreviations: PMD, post-mortem delay.

Comment [GC]: I take it that CERAD criteria weren't available for the Manchester cases?

Comment [GC]: