Online supplement

Participants

Exclusion criteria for the study included: schizophrenia; depression (15-item Geriatric Depression Scale score ≥ 6);[11] Parkinson's disease; cancer (except basal cell skin carcinoma) within the past 2 years; symptomatic stroke; uncontrolled diabetes; current regular alcohol use exceeding two standard drinks per day for women or four per day for men. For each assessment, a clinical review panel considered all available medical, psychiatric and neuropsychological information to confirm the cognitive health of each participant.

Selection of healthy older adults into the full AIBL cohort was controlled to ensure: (a) a wide age distribution from 60 years through to very elderly individuals and (b) that approximately 50% had a subjective memory complaint; for the 25% of this cohort who completed PiB imaging, an additional criterion was added to enrich the sample with *APOE* ε4 carriers: (c) that approximately 50% of the sample were *APOE* ε4 carriers. The study was approved by and complied with the regulations of the institutional research and ethics committees of Austin Health, St Vincent's Health, Hollywood Private Hospital and Edith Cowan University. All participants provided written informed consent prior to participating in the study.

Neuropsychological assessment

The episodic memory composite score was comprised of scores on the California Verbal Learning Test – Second Edition (CVLT-II)[12] delayed recall and Rey Complex Figure Test (RCFT)[13] 30 min delayed recall tests. The verbal memory composite score was comprised of scores on logical memory delayed recall, CVLT-II delayed recall, and CVLT-II d' measures. The visual memory composite score was comprised of scores on the RCFT 3 min delayed recall, RCFT 30 min delayed recall and RCFT recognition tests. The executive function composite score was comprised of scores on the Stroop Colors/Dots, Letter Fluency (FAS) and Category Switching (Fruit/Furniture) tests from the Delis-Kaplan Executive Function System (D-KEFS). The language composite score was comprised of scores on the D-KEFS Category Fluency (Animals/Boys' Names) and Boston Naming[14] tests. The attention composite score was comprised of scores on the Digit Span,[15] Stroop Dots[16] and Digit Symbol Coding[15] tests. The visuospatial composite score was comprised of scores on the RCFT Copy and Clock Drawing[17] tests. Factor analyses revealed strong loadings (i.e. all factor loadings ≥ 0.47) of each of the component measures on these composite scores.

Additional references

11 Sheikh JI, Yesavage JA. Geriatric Depression Scale (GDS): recent evidence and development of a shorter version. *Clin Gerontol* 1986; **5**: 165–73.

12 Delis DC, Kramer JH, Kaplan E, Ober BA. *California Verbal Learning Test: Second Edition*. Psychological Corporation, 2000.

13 Meyers JE, Meyers KR. *Rey Complex Figure Test And Recognition Trial: Professional Manual*. PAR Inc, 1996.

14 Saxton J, Ratcliff G, Munro CA, Coffey EC, Becker JT, Fried L, et al. Normative data on the Boston Naming Test and two equivalent 30-item short forms. *Clin Neuropsychol* 2000; **14**: 526–34.

15 Wechsler D. *Wechsler Adult Intelligence Scale (3rd edn) (WAIS-III)*. Psychological Corporation, 1997.

16 Strauss E, Sherman EMS, Spreen O. *A Compendium of Neuropsychological Tests: Administration, Norms, and Commentary* (3rd edn). Oxford University Press, 2006.

17 Shulman KI, Gold DP, Cohen CA, Zucchero CA. Clock drawing and dementia in the community: a longitudinal study. *Int J Geriatr Psychiatry* 1993; **8**: 487–96.

18 Wechsler D. *Wechsler Test of Adult Reading: Examiner's Manual*. Psychological Corporation, 2001.

19 Folstein MF, Folstein SE, McHugh PR. 'Mini-mental state': a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975; **12**: 189–98.

Table DS1 Sample characteristics (*n* = 178)

Characteristic	*n* (%)	Mean (s.d.)
Age, years		71.5 (7.4)
Female gender	89 (50.0)	
Education		
≤ 12 years	83 (46.6)	
13+ years	95 (53.4)	
Wechsler Adult Reading Test IQ[18]		111.7 (6.7)
Mini-Mental State Examination[19]		28.7 (1.2)
Pittsburgh Compound B Standardised Uptake Value Ratio >1.5	55 (30.9)	
Apolipoprotein E (*APOE*) ε4 carrier	72 (40.5)	
Hospital Anxiety and Depression Scale, anxiety score		4.1 (2.8)
Positive screen for anxiety	23 (12.9)	
Hospital Anxiety and Depression Scale, depression score		2.8 (2.3)
Positive screen for depression	8 (4.5)	
Subjective memory complaint	95 (53.4)	

Table DS2 Results of linear mixed-effects models examining the relation between cerebral beta-amyloid, anxiety and depressive symptoms, and cognitive outcomes over a 3-year period[a]

	Episodic memory		Verbal memory		Visual memory		Attention		Language		Visuospatial		Executive	
	F	P	F	P	F	P	F	P	F	P	F	P	F	P
PiB SUVR >1.5	1.74	0.19	5.45	0.020	1.72	0.19	0.01	0.94	0.08	0.77	0.01	0.94	0.02	0.90
Anxiety symptoms	0.01	0.99	2.08	0.15	0.15	0.70	4.96	0.026	0.01	0.98	0.29	0.59	3.95	0.047
Depressive symptoms	0.07	0.79	0.01	0.93	0.31	0.58	0.07	0.79	3.74	0.06	0.31	0.58	1.02	0.31
Time	12.85	<0.001	20.67	<0.001	0.32	0.57	3.95	0.048	4.64	0.032	30.42	<0.001	5.82	0.016
PiB × anxiety symptoms	1.69	0.19	4.98	0.026	1.75	0.19	1.78	0.18	0.01	0.95	0.98	0.32	0.20	0.65
PiB × depressive symptoms	2.63	0.11	0.20	0.66	3.43	0.07	1.72	0.19	3.07	0.08	0.27	0.60	0.56	0.46
PiB × time	15.15	<0.001	20.54	<0.001	4.60	0.033	0.01	0.91	0.87	0.35	0.46	0.50	0.01	0.91
Anxiety symptoms × time	1.82	0.18	2.20	0.14	0.11	0.74	2.04	0.15	0.01	0.99	0.56	0.45	4.41	0.037
Depressive symptoms × time	0.19	0.66	0.01	0.94	0.01	0.99	0.34	0.56	0.42	0.51	0.05	0.83	0.01	0.97
PiB × time × anxiety symptoms	4.20	0.041	3.97	0.047	1.26	0.26	1.74	0.19	0.06	0.81	0.97	0.33	1.17	0.28
PiB × time × depressive symptoms	1.26	0.26	0.28	0.59	1.14	0.29	0.15	0.70	2.22	0.14	0.17	0.68	0.01	0.94

PiB, ^{11}C-Pittsburgh Compound B; PiB SUVR, PiB standardised uptake value ratio.
a. The PiB level reflects mean of beta-amyloid in frontal, post-cingulate, lateral temporal and occipital cortices. Adjusted for age, education, IQ, apolipoprotein E (*APOE*) genotype and subjective memory complaint.

Table DS3 Adjusted slope estimates by ^{11}C-Pittsburgh Compound B (PiB) and anxiety group[a]

	Mean (s.e.)				Pair-wise comparisons
	PiB−/Anxiety−	PiB−/Anxiety+	PiB+/Anxiety−	PiB+/Anxiety+	
Episodic memory	0.14 (0.09)	0.26 (0.25)	−0.29 (0.14)	−0.65 (0.35)	3,4<1; 4<3
Verbal memory	0.18 (0.09)	0.21 (0.25)	−0.32 (0.14)	−0.93 (0.34)	3,4<1; 4<3

a. The PiB level reflects mean of beta-amyloid in frontal, post-cingulate, lateral temporal and occipital cortices.