Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix. Methods

Neuropsychological scores

To obtain robust proxies of cognitive abilities and minimize the issue of multiple statistical testing, composite scores were used for each cognitive domain, instead of multiple (sub)tests. For that purpose, performance on various cognitive tests were z-transformed and averaged as follows. Please note that before averaging, Z-scores derived from reaction times and percentages/number of error were reversed so that increasing values always indicated better performance.

- Processing speed
  - Time to perform the Trail Making test (TMT) part A.
  - Time to complete the word card from the Stroop test (reading condition).
  - Time to complete the color card from the Stroop test (naming condition).

- Attention
  - Attention sub-score from the Mattis Dementia Rating Scale.
  - Number of correct items at the D2R test.
  - Percentage of errors at the D2R test.

- Executive functions
  - TMT test (time difference between TMT part B and part A, divided by the time to perform part A).
  - Stroop test (time difference between the interference and naming conditions).
  - Verbal fluency (number of words beginning with ''p'' in 2 min).

- Working memory
  - Digit span forward from the WAIS IV.
  - Digit span backward from the WAIS IV.
  - Digit span forward + backward total raw note from the WAIS IV.

- Episodic memory
  - Memory subscore from the Mattis Dementia Rating Scale.
  - Sum of the five free recalls from the learning trials of the California Verbal Learning Test (CVLT).
  - Short-term free recall from the CVLT.
  - Long-term free recall from the CVLT.
  - Long-term free recall from the Logical Memory Story test from the WMS IV.

Abbreviations: CVLT, California Verbal Learning Test; TMT, Trail Making Test; WAIS, Wechsler Adult Intelligence Scale; WMS, Weschler Memory Scale.

Neuroimaging procedure

All participants were scanned at the Cyceron Center (Caen, France) on the same MRI (Philips Achieva 3.0T scanner) and PET (Discovery RX VCT 64 PET-CT scanner, General Electric Healthcare) cameras. During the MRI session, subjects were equipped with earplugs and their head was stabilized with foam pads in order to minimize head motion.

1. *Structural MRI*

A high-resolution T1-weighted anatomical image was acquired using a 3D fast-field echo sequence (3D-T1-FFE sagittal, repetition time =7.1 ms, echo time = 3.3 ms, flip angle = 6°, 180 slices with no gap, slice thickness = 1mm, field of view = 256x256 mm², in-plane resolution= 1x1x1 mm³). T1-weighted images were segmented using FLAIR images (3D-IR sagittal, TR/TE/TI = 4800/272/1650 ms ; flip angle = 40°; 180 slices with no gap; slice thickness = 1 mm; field of view = 250x250 mm²; in-plane resolution = 0.98x0.98 mm²), spatially normalized to the Montreal Neurological Institute (MNI) template, modulated using the SPM12 segmentation procedure (http://www.fil.ion.ucl.ac.uk) and smoothed with an 8 mm full-width at half-maximum (FWHM) Gaussian filter. Images were then masked to exclude non-grey matter voxels from the analyses.

2. *PET imaging*

Florbetapir- and FDG-PET scans were acquired in two separate sessions with a resolution of $3.76 \times 3.76 \times 4.9$ mm^3 (field of view = 157 mm). Forty-seven planes were obtained with a voxel size of $1.95 \times 1.95 \times 3.27$ mm^3. A transmission scan was performed for attenuation correction before the PET acquisition.

For the Florbetapir-PET scan, each participant underwent a 10 min PET scan beginning at the intravenous injection of ~4MBq/Kg of Florbetapir, and a 10 min PET scan beginning 50 min after the intravenous injection. Early Florbetapir-PET, reflecting brain perfusion, was reconstructed from 1 to 6 min. Late-Florbetapir acquisition reflected brain amyloid burden.

For the FDG-PET scan, participants (n=87) were fasted for at least 6 hours before scanning. After a 30-min resting period in a quiet and dark environment, 180 MBq of ^{18}F-fluorodeoxyglucose were intravenously injected as a bolus. A 10-min PET acquisition scan began 50 min after injection.

PET images were coregistered on their corresponding anatomical MRI, voxel-wise corrected for partial volume effects using the three-compartmental voxel-wise Müller-Gärtner method[1], and were then normalized to the MNI template using deformation parameters derived from the anatomical MRI. Resulting images were scaled using cerebellar grey matter as a reference. A smoothing kernel of 10 mm Gaussian filter was applied and images were masked to exclude non-grey matter voxels from the analyses. PVE-corrected normalized and scaled Florbetapir-PET images were also used to extract the individual global cortical amyloid standard uptake value ratio (SUVr) using a predetermined neocortical mask including the entire grey matter, except the cerebellum, occipital and sensory motor cortices, hippocampi, amygdala and basal nuclei[2]. The threshold for amyloid positivity was defined as >0.99, and corresponded to the 99.9[th] percentile of the neocortical SUVr distribution among 45 healthy young individuals, aged <40 years.

Polysomnography recording

Twenty EEG electrodes were placed over the scalp (Fp1, Fp2, F3, F4, F7, F8, Fz, C3, C4, Cz, T3, T4, P3, P4, Pz, O1, O2, vertex ground, and a bi-mastoid reference) according to the international 10-20 system, with impedances kept below 5 kΩ. Participants also underwent an electrooculogram, electrocardiogram, and chin electromyogram. Respiratory movements, airflow, and oxygen saturation were recorded respectively with thoracic and abdominal belts, nasal and oral thermistors, and a finger pulse oximeter. The EEG signal was digitalized at a sampling rate of 256 Hz. High-pass and low-pass filters were applied, respectively at 0.3Hz and 35Hz.

eTable 1. Detailed statistics of significant neuroimaging clusters.

Brain areas	Cluster extent		MNI coordinates			T-value	$p_{FWE\text{-}corrected}$	Effect size (Cohen's d)
	voxels	mm³	x	y	z			
MRI								
B precuneus, posterior cingulate	829	2 798	0	-63	20	4.12	.04	.75
Early Florbetapir-PET								
L calcarine, L lingual, B precuneus, B posterior and middle cingulate	3 946	13 318	-6	-76	6	4.62	.001	.86
FDG-PET								
B calcarine, B lingual, B precuneus, B posterior cingulate	4 295	14 496	-3	-68	12	4.63	.001	1.04
Late Florbetapir-PET								
L calcarine, L precuneus, L posterior cingulate, L cuneus	4 699	15 859	-10	-78	6	4.51	.04	.83

Abbreviations: B, bilateral; FDG, ^{18}F-fluorodeoxyglucose, L, left; MNI, Montreal Neurological Institute; MRI: magnetic resonance imaging.
Results were obtained at a p<0.005 (uncorrected) threshold and only clusters surviving a FWE cluster-level correction are reported.

eTable 2. Results of inter-modality correlations.

Neuroimaging modality		Brain perfusion	Amyloid	Glucose metabolism	GM volume
Brain perfusion	Pearson's r	—			
	p-value	—			
	Upper 95% CI	—			
	Lower 95% CI	—			
Amyloid	Pearson's r	0.34	—		
	p-value	<.001	—		
	Upper 95% CI	0.49	—		
	Lower 95% CI	0.18	—		
Glucose metabolism	Pearson's r	0.70	0.15	—	
	p-value	<.001	.17	—	
	Upper 95% CI	0.80	0.35	—	
	Lower 95% CI	0.58	-0.06	—	
GM volume	Pearson's r	0.59	0.21	0.4	—
	p-value	<.001	.02	<.001	—
	Upper 95% CI	0.69	0.37	0.56	—
	Lower 95% CI	0.46	0.03	0.21	—

Neuroimaging signal values were extracted from significant clusters obtained in voxel-wise between-group comparisons. Please note that results remained unchanged when controlling for age, sex, education, body mass index, sleep medication use and APOE4 status (data not shown).

eTable 3. Results of between-group comparisons using a ROI approach for PET data.

Imaging modality	Region of Interest	F	p	Partial eta-squared
Late Florbetapir-PET (PVE-corrected)	**Composite**	**4.77**	**.03**	**0.04**
	PCC L	**4.88**	**.03**	**0.04**
	PCC R	**4.62**	**.03**	**0.04**
	Cuneus L	**7.07**	**.01**	**0.06**
	Cuneus R	**5.35**	**.02**	**0.04**
	Precuneus L	**4.23**	**.04**	**0.04**
	Precuneus R	**4.17**	**.04**	**0.03**
	Lingual L	**5.38**	**.02**	**0.04**
	Lingual R	0.66	.42	0.01
	Calcarine L	**8.81**	**.004**	**0.07**
	Calcarine R	3.45	.07	0.03
Late Florbetapir-PET (uncorrected for PVE)	Composite	3.85	.05	0.03
	PCC L	1.94	.17	0.02
	PCC R	1.59	.21	0.01
	Cuneus L	3.58	.06	0.03
	Cuneus R	**4.21**	**.04**	**0.04**
	Precuneus L	**4.03**	**.05**	**0.03**
	Precuneus R	3.85	.05	0.03
	Lingual L	**4.26**	**.04**	**0.04**
	Lingual R	2.61	.11	0.02
	Calcarine L	3.68	.06	0.03
	Calcarine R	3.59	.06	0.03
Early Florbetapir-PET (PVE-corrected)	**Composite**	**9.12**	**.003**	**0.07**
	PCC L	**8.90**	**.004**	**0.07**
	PCC R	**10.55**	**.002**	**0.08**
	Cuneus L	**4.88**	**.03**	**0.04**
	Cuneus R	3.00	.09	0.03
	Precuneus L	**6.34**	**.01**	**0.05**
	Precuneus R	**7.98**	**.01**	**0.06**
	Lingual L	**8.00**	**.01**	**0.06**
	Lingual R	**5.35**	**.02**	**0.04**
	Calcarine L	**12.50**	**.001**	**0.10**
	Calcarine R	**4.05**	**.05**	**0.03**
Early Florbetapir-PET (uncorrected for PVE)	**Composite**	**6.74**	**.01**	**0.06**
	PCC L	**7.41**	**.01**	**0.06**
	PCC R	**9.12**	**.003**	**0.07**
	Cuneus L	3.52	.06	0.03
	Cuneus R	2.90	.09	0.02
	Precuneus L	**5.23**	**.02**	**0.04**
	Precuneus R	**6.17**	**.01**	**0.05**
	Lingual L	**7.27**	**.01**	**0.06**
	Lingual R	**5.27**	**.02**	**0.04**
	Calcarine L	**8.58**	**.004**	**0.07**
	Calcarine R	**4.17**	**.04**	**0.04**
FDG-PET (PVE-corrected)	**Composite**	**6.98**	**.01**	**0.08**
	PCC L	**9.39**	**.003**	**0.11**
	PCC R	**10.31**	**.002**	**0.12**
	Cuneus L	**5.99**	**.02**	**0.07**
	Cuneus R	**5.28**	**.02**	**0.06**
	Precuneus L	**4.60**	**.04**	**0.06**
	Precuneus R	**5.70**	**.02**	**0.07**
	Lingual L	**4.90**	**.03**	**0.06**

	Lingual R	3.22	.08	0.04
	Calcarine L	**9.05**	**.004**	**0.10**
	Calcarine R	**4.13**	**.05**	**0.05**
FDG-PET (uncorrected for PVE)	**Composite**	**5.04**	**.03**	**0.06**
	PCC L	**7.78**	**.007**	**0.09**
	PCC R	**8.48**	**.005**	**0.10**
	Cuneus L	**4.69**	**.03**	**0.06**
	Cuneus R	**4.62**	**.04**	**0.06**
	Precuneus L	**4.01**	**.05**	**0.05**
	Precuneus R	**5.03**	**.03**	**0.06**
	Lingual L	3.56	.06	0.04
	Lingual R	2.68	.10	0.03
	Calcarine L	**5.62**	**.02**	**0.07**
	Calcarine R	3.66	.06	0.04

Abbreviations: AAL, Automated Anatomical Labelling; FDG, ^{18}F-fluorodeoxyglucose, L, left; PCC, posterior cingulate cortex; PVE, partial volume effect; R, right; ROI, region of interest.

Results of between-group comparisons (SDB+>SDB-) for amyloid burden (late Florbetapir-PET, n=125), brain perfusion (early Florbetapir-PET, n=124) and glucose metabolism (FDG-PET, n=87) data, extracted from PVE-corrected and uncorrected PET images in standardized ROIs of the AAL Atlas overlapping with the significant clusters obtained in the voxel-wise analyses. The "composite" ROI is a meta-ROI comprising all the individual AAL ROIs listed below (i.e., left and right PCC, cuneus, precuneus, lingual and calcarine regions). The statistical threshold for significance was set to p<0.05, and significant results are indicated in bold.

eTable 4. Results of complementary forward stepwise regression analyses.

Imaging modality	Model	Predictor	Unstandardized coefficient	Standardized coefficient	R²	p	Lower 95% CI	Upper 95% CI
Neocortical amyloid SUVr	1	(Intercept)	0.97			<.001	0.94	1.01
		Hypoxia composite	0.06	0.23	0.05	.01	0.01	0.11
	2	(Intercept)	0.95			<.001	0.91	0.99
		Hypoxia composite	0.06	0.22		.02	0.01	0.10
		ApoE4 status	0.09	0.19	0.09	.04	0.01	0.17
	Full model				*0.13*	*.07*		
GM volume extracted from the composite AAL ROI	1	(Intercept)	0.72			< .001	0.68	0.76
		BMI	-0.003	-0.32	0.10	< .001	-0.004	-0.001
	2	(Intercept)	0.72			< .001	0.69	0.76
		BMI	-0.002	-0.31		< .001	-0.004	-0.001
		Sex	-0.02	-0.24	0.15	.01	-0.03	-0.005
	3	(Intercept)	0.83			< .001	0.72	0.94
		BMI	-0.003	-0.32		< .001	-0.004	-0.001
		Sex	-0.02	-0.23		.01	-0.03	-0.005
		Age	-0.002	-0.17	0.19	.05	-0.003	-6.404e -6
	4	(Intercept)	0.85			< .001	0.73	0.96
		BMI	-0.003	-0.34		< .001	-0.004	-0.001
		Sex	-0.02	-0.26		.002	-0.03	-0.007
		Age	-0.002	-0.19		.03	-0.003	-1.975e -4
		AHI	0.007	0.19	0.22	.03	6.235e -4	0.01
	Full model				*0.25*	*<.001*		

Abbreviations: AAL, Automated Anatomical Labelling; ROI, Region of Interest; SUVr, Standard Uptake Value ratio.

eTable 5. Results of partial correlation analyses between SDB parameters and SDB-related brain changes with cognitive and behavioural scores.

Cognitive and behavioral variables	SDB parameters			SDB-related brain changes			
	AHI (n=127)	Fragmentation composite (n=127)	Hypoxia composite (n=118)	Perfusion (n=124)	Metabolism (n=87)	Amyloid burden (n=125)	GM volume (n=127)
Mattis Dementia Rating Scale	r=.83	r=.06	r=.003	r=.02	r=.03	r=.07	r=-.10
	p=.38	p=.51	p=.98	p=.86	p=.78	p=.44	p=.30
Attention	r=.06	r=.07	r=.02	r=.16	r=-.01	r=.07	r=.06
	p=.54	p=.49	p=.80	p=.08	p=.91	p=.44	p=.529
Processing speed	r=-.02	r=.003	r=.03	r=.04	r=.05	r=.02	r=-.05
	p=.88	p=.98	p=.75	p=.66	p=.69	p=.84	p=.63
Working memory	r=-.01	r=-.03	r=-.005	r=-.007	r=.04	r=-.11	r=-.02
	p=.91	p=.76	p=.96	p=.94	p=.76	p=.22	p=.80
Executive functions	r=-.06	r=-.07	r=-.16	r=.08	r=.11	r=-.09	r=-.01
	p=.51	p=.45	p=.09	p=.41	p=.35	p=.34	p=.90
Episodic memory	r=-.09	r=-.12	r=-.17	r=-.05	r=-.08	r=-.19	r=-.12
	p=.35	p=.20	p=.08	p=.59	p=.50	p=.04	p=.21
Cognitive Difficulties Scale	r=.06	r=.04	r=.09	r=.07	r=-.03	r=-.06	r=.12
	p=.53	p=.69	p=.35	p=.47	p=.80	p=.52	p=.18
Pittsburgh Sleep Quality Index	r=.14	r=.03	r=-.03	r=.11	r=.07	r=.05	r=.22
	p=.14	p=.78	p=.73	p=.23	p=.55	p=.61	p=.02
Epworth sleepiness scale	r=-.04	r=-.03	r=-.03	r=.13	r=.08	r=.05	r=.06
	p=.69	p=.75	p=.76	p=.17	p=.49	p=.60	p=.52

Abbreviations: AHI, apnea-hypopnea index; ApoE, apolipoprotein E; GM, gray matter; SDB, sleep-disordered breathing.
Partial correlations were adjusted for age, sex, education, body mass index, sleep medication use and ApoE4 status. R values correspond to partial correlation coefficients, and results were considered significant at p<0.0008, after applying a Bonferroni correction for multiple testing (p=0.05/63).

eReferences.

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