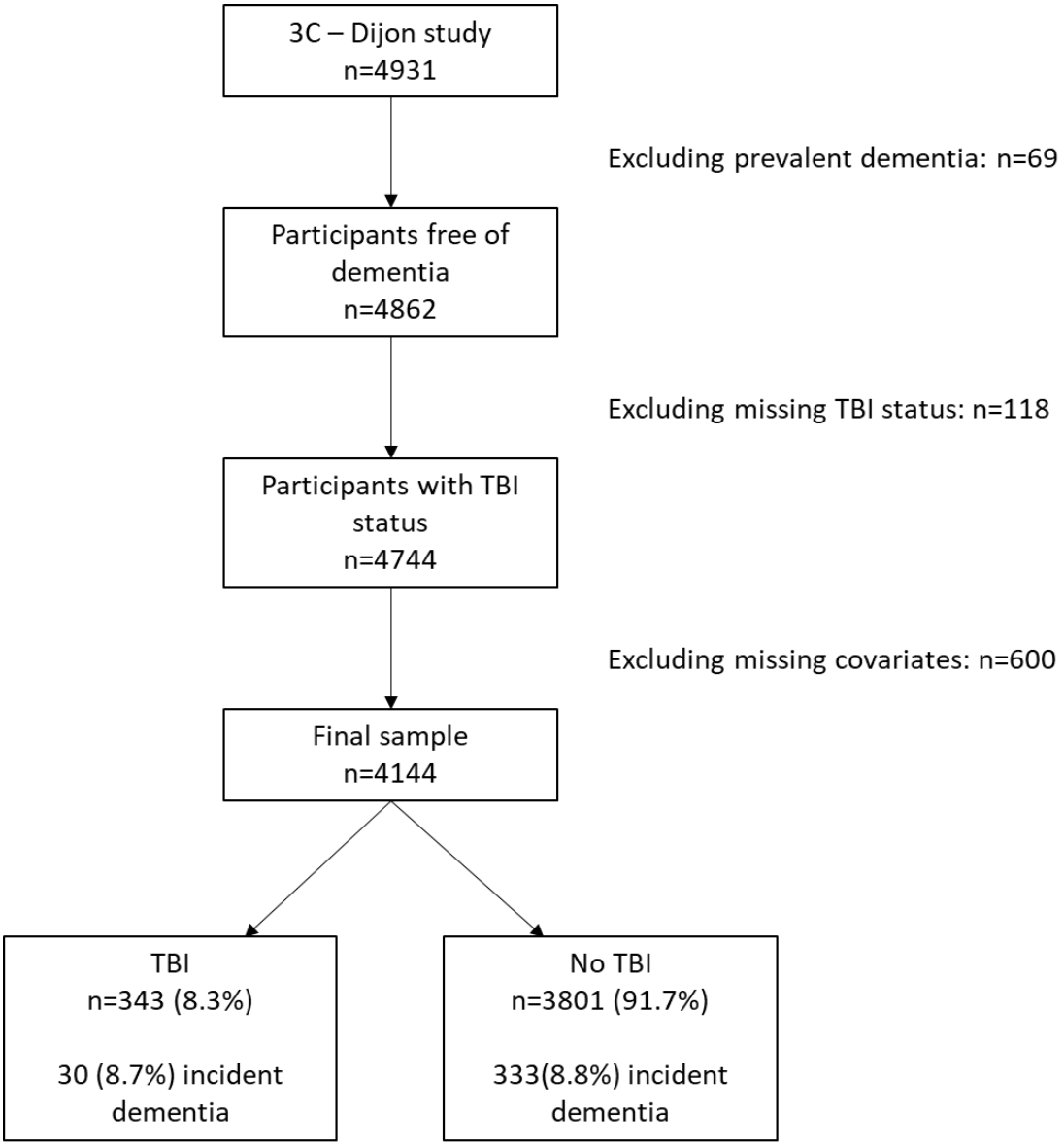
Supplementary Material

How Traumatic Brain Injury History Relates to Brain Health MRI Markers and Dementia Risk: Findings from the 3C Dijon Cohort

Supplementary Figure 1. Flow chart describing selection into study sample



Supplementary Table 1. Baseline characteristics of study participants included in the incidence analysis sample and excluded because of missing TBI status and missing covariates, the Three City – Dijon study, 1999–2000

	Included (n=4,144)	Excluded (n=718)	p
Women n (%)	2,543 (61.4)	462 (64.3)	0.13
Age, mean (SD)	74.3 (5.5)	76.2 (6.4)	<0.001
Education level			0.02
Missing data, n	*0*	*8*	
Less than high school n (%)	2,634 (63.6)	483 (68.0)	
High school and above n (%)	1,510 (36.4)	227 (32.0)	
APOE ε4	869 (21.0)	86 (21.4)	0.84
Missing data, n	*0*	*316*	
Height (cm), mean (SD)	161.9 (0.88)	161.8 (0.84)	0.83
Missing data, n	*0*	*21*	
Hypertension	3,296 (79.4)	585 (81.8)	0.16
Missing data, n	*0*	*3*	
Stroke history	192 (4.6)	53 (8.3)	<0.001
Missing data, n	*0*	*81*	
CVD history	605 (14.6)	99 (18.2)	0.03
Missing data, n	*0*	*175*	
Diabetes	387 (9.3)	65 (15.3)	<0.001
Missing data, n	*0*	*294*	
High depressive symptoms	865 (20.9)	185 (29.7)	<0.001
Missing data, n	*0*	*94*	
IADL dependency	370 (9.0)	133 (18.9)	<0.001
Missing data, n	*28*	*13*	
Low MMSE score	193 (4.7)	65 (9.1)	<0.001
Missing data, n	*8*	*6*	

TBI, traumatic brain injury; CVD, cardiovascular disease; IADL, Instrumental activities of daily living; MMSE: Mini-Mental State Examination

Supplementary Table 2. Baseline characteristics of study participants included and excluded in the MRI analysis sample*, the Three City – Dijon study, 1999–2000

	Included (n=1,675)	Excluded (n=2,443)	p
Women n (%)	1,006 (60.1)	1,551 (63.5)	0.03
Age, mean (SD)	72.1 (3.8)	73.2 (4.0)	<0.001
Education level			<0.001
Missing data, n	*0*	*7*	
Less than high school n (%)	1,007 (60.1)	1,628 (66.8)	
High school and above n (%)	668 (39.9)	808 (33.2)	
APOE ε4	370 (22.1)	474 (21.4)	0.60
Missing data, n	*0*	*226*	
Height (cm), mean (SD)	162.5 (8.9)	161.6 (8.6)	<0.001
Missing data, n	*0*	*8*	
Hypertension	1,283 (76.6)	1,936 (79.3)	0.04
Missing data, n	*0*	*1*	
Stroke history	68 (4.1)	115 (4.8)	0.24
Missing data, n	*0*	*64*	
CVD history	184 (11.0)	343 (14.9)	<0.001
Missing data, n	*0*	*135*	
Diabetes	142 (8.5)	246 (11.0)	0.009
Missing data, n	*0*	*208*	
High depressive symptoms	164 (9.8)	287 (12.1)	0.02
Missing data, n	*0*	*61*	
IADL dependency	68 (4.1)	208 (8.6)	<0.001
Missing data, n	*15*	*17*	
Low MMSE score	49 (2.9)	138 (5.7)	<0.001
Missing data, n	*3*	*8*	

TBI, traumatic brain injury; CVD, cardiovascular disease; IADL, Instrumental activities of daily living; MMSE, Mini-Mental State Examination
*participants eligible for MRI among the population <80 years old

Supplementary Table 3. Associations* between history of TBI and risk of dementia and Alzheimer's disease after imputation of adjustment variables missing data, the Three City – Dijon study, 1999-2011

	All Dementia	**Alzheimer's disease dementia**
	HR (95% CI)	HR (95% CI)
Model 1		
TBI history versus not	0.96 (0.69 – 1.34)	0.97 (0.68 – 1.37)
Model 2		
TBI history versus not	0.88 (0.63 – 1.24)	0.88 (0.61 – 1.28)

TBI, traumatic brain injury

Model 1 adjusted for sex. Model 2: model 1 + education, *APOE* ε4 status, height, stroke history, non-stroke CVD history, diabetes, hypertension, and high depressive symptoms.

* Using Illness-death models

Supplementary Table 4. Associations* between history of TBI and risk of dementia and Alzheimer's disease, after exclusion of individuals with MMSE scores < 27

	All Dementia		Alzheimer's disease dementia	
	HR (95% CI)	p	HR (95% CI)	p
Model 1				
TBI history versus not	1.16 (0.70 – 1.92)	0.56	1.46 (0.87 – 2.43)	0.15
Model 2				
TBI history versus not	0.99 (0.45 – 2.18)	0.98	1.21 (0.65 – 2.27)	0.55

TBI, traumatic brain injury

Model 1 adjusted for sex. Model 2: model 1 + education, *APOE* ε4 status, height, stroke history, non-stroke CVD history, diabetes, hypertension, and high depressive symptoms.

* Using Illness-death models

Supplementary Table 5. Association* between history of TBI and MRI brain markers, stratified by sex, *APOE* ε4 status, and education level, the Three City – Dijon study, 1999-2011

	β (95% CI)	β (95% CI)	Interaction p
Brain parenchymal fraction			
Sex	**Men**	**Women**	0.51
TBI history versus not	-0.14 (-0.91, 0.64)	-0.45 (-1.14, 0.24)	
Education level	**< than High school**	**High school and more**	0.78
TBI history versus not	-0.30 (-0.99, 0.39)	-0.41 (-1.20, 0.38)	
***APOE* ε4**	**Non *APOE* ε4 carriers**	***APOE* ε4 carriers**	0.42
TBI history versus not	-0.24 (-0.82, 0.34)	-0.85 (-2.00, 0.31)	
Grey matter volume			
Sex	**Men**	**Women**	0.54
TBI history versus not	-4.03 (-15.64 ,7.57)	0.72 (-8.07, 9.51)	
Education level	**< than High school**	**High school and more**	0.54
TBI history versus not	-0.22 (-9.63, 9.19)	-3.82 (-14.39, 6.74)	
***APOE* ε4**	**Non *APOE* ε4 carriers**	***APOE* ε4 carriers**	0.40
TBI history versus not	0.07 (-7.55, 7.92)	-6.55 (-23.13, 10.02)	
White matter volume			
Sex	**Men**	**Women**	0.33
TBI history versus not	-11.78 (-25.17, 1.60)	-3.08 (-12.70, 6.55)	
Education level	**< than High school**	**High school and more**	0.47
TBI history versus not	-9.09 (-19.66, 1.46)	-3.17 (-15.03, 8.70)	
***APOE* ε4**	**Non *APOE* ε4 carriers**	***APOE* ε4 carriers**	0.60
TBI history versus not	-5.26 (-14.02, 3.51)	-9.84 (-27.27, 8.11)	
Hippocampal volume			
Sex	**Men**	**Women**	0.79
TBI history versus not	-0.03 (-0.24, 0.18)	0.004 (-0.15, 0.15)	
Education level	**< than High school**	**High school and more**	0.49
TBI history versus not	0.022 (-0.14, 0.19)	-0.071 (-0.26, 0.12)	
***APOE* ε4**	**Non *APOE* ε4 carriers**	***APOE* ε4 carriers**	0.33
TBI history versus not	0.019 (-0.12, 0.16)	-0.11 (-0.39, 0.18)	
WMHV			
Sex	**Men**	**Women**	0.99
TBI history versus not	-0.10 (-0.28, 0.09)	-0.09 (-0.23, 0.06)	
Education level	**< than High school**	**High school and more**	0.06
TBI history versus not	-0.16 (-0.31, -0.01)	0.04 (-0.13, 0.22)	
***APOE* ε4**	**Non *APOE* ε4 carriers**	***APOE* ε4 carriers**	0.38
TBI history versus not	-0.10 (-0.23, 0.02)	0.01 (-0.23, 0.26)	
CBI			
Sex	**Men**	**Women**	0.71
TBI history versus not	1.14 (0.47 – 2.45)	0.80 (0.29 – 1.87)	
Education level	**< than High school**	**High school and more**	0.45
TBI history versus not	1.14 (0.52 – 2.29)	0.66 (0.19 – 1.80)	
***APOE* ε4**	**Non *APOE* ε4 carriers**	***APOE* ε4 carriers**	0.22

TBI history versus not	0.77 (0.34 – 1.55)	1.87 (0.57 – 5.25)

TBI, traumatic brain injury; WMHV, white matter hyperintensities volume; CBI, covert brain infarct

* Using Illness-death models in model 2 (adjusted for sex, education, *APOE* ε4 status, height, stroke history, non-stroke CVD history, diabetes, hypertension, and high depressive symptoms.) For CBI, Odd ratios and 95% CI are presented.