Supplementary Online Content

Lee JK, Wu J, Bullen J, et al. Association of cavum septum pellucidum and cavum vergae with cognition, mood, and brain volumes in fighters. *JAMA Neurol.* Published online September 9, 2019. doi:10.1001/jamaneurol.2019.2861

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

eAppendix 1. Professional Fighters Brain Health Study

Fighters who enrolled in the study were required to hold a Nevada state license to fight professionally. Study participants also needed to be at least 18 years of age with at least a fourth-grade reading level, fluency in English or Spanish, and a willingness to undergo annual evaluations including 3T brain MRI and blood sampling for genotyping and exploratory biomarker studies. Fighters also completed a structured interview to provide demographic information such as age; years of education; and fight exposure data, such as type of fighter (boxer or mixed martial arts), total number of fights, and years of fighting. Information about race and ethnicity was obtained as defined by the participants and was assessed in case these factors were found to be important variables in predicting injury in fighters. Longitudinal yearly follow-up with repeat imaging is also ongoing, with approximately 40% of fighters participating.

Control participants who enrolled in the study were matched with fighters by age and sex and were required to have no history of trauma (including military service or participation in a sport associated with head injuries such as boxing, football, rugby, hockey, mixed martial arts, wrestling, soccer, or rodeo in high school and beyond).

Medical history was self-reported by both fighters and control participants and included any diagnosed medical conditions; previous surgeries; use of medications, performance-enhancing drugs, or other supplements; and history of recreational drug use.

eAppendix 2. Cognitive and Mood Assessments

Mood assessments included tests of depression, impulsivity, and sleepiness. The Barrett Impulsiveness Scale, which consists of 30 questions, was used to assess impulsivity in relation to attention, cognitive instability, motor, perseverance, self-control, and cognitive complexity.[1] Fighters also completed the Epworth Sleepiness Scale, which consists of 8 questions on a 4-point scale evaluating for sleepiness (and distinguishing between sleepiness and feelings of fatigue and weariness).[2] Lastly, fighters completed the Patient Health Questionnaire depression scale, which consists of 10 questions to evaluate for depression severity ranging from minimal to severe depression.[3]

Cognition was assessed using raw scores from CNS Vital Signs (CNS Vital Signs, North Carolina).[4] This is a computerized test that was used to obtain robust and reliable measurements of cognition in the clinical realms of verbal memory, processing speed, psychomotor speed, and reaction time. As part of the CNS Vital Signs evaluation, psychomotor speed was calculated as the finger tapping test right taps average plus the finger tapping test left taps average plus the number of correct responses on the symbol digit coding test; processing speed was calculated as the number of correct responses on the symbol digit coding test minus the number of errors on this test.

eAppendix 3. Imaging

Conventional sagittal 3D magnetization-prepared rapid acquisition with gradient echo (MPRAGE) T1 (voxel size = 1 × 1 × 1.2 mm; flip angle/repetition time [TR]/echo time [TE]/inversion time [TI] = 9/2300/2.98/900 ms; scan time = 9:14), axial turbo spin-echo (TSE) T2 (voxel size = 0.8 × 0.8 × 4 mm; TR/TE =5000/84 ms; 38 slices; scan time = 0:57), axial TSE fluid-attenuated inversion recovery (voxel size = 0.8 × 0.8 × 4 mm; TR/TE/TI = 7000/81/2220 ms; 38 slices; scan time = 2:36), and axial susceptibility weighted imaging (SWI) (voxel size = 0.9 × 0.9 × 0.9 mm; TR/TE = 20/27 ms; 36 slices; scan time = 1:17) sequences were used for this study. These sequences have previously been used to identify the presence of cerebral microhemorrhages (CMHs), cavum septum pellucidum (CSP), cavum vergae (CV), and nonspecific white matter changes (WMCs).[5] During this previous analysis, 5 neuroradiologists evaluated for the presence of CMHs and 1 neuroradiologist evaluated for the presence of CSP/CV. CSPs were included only if they measured > 2 mm in length. WMCs were excluded if they were < 3 mm or if they were associated with another abnormality such as a CMH or encephalomalacia. CMHs were well-defined areas of abnormal susceptibility hypointensity that were focal, rounded, < 5 mm, not on the pial or ependymal surface, and not caused by vessel or normal variants such as developmental venous anomalies. Cavernous malformations were also excluded from this definition on the basis of characteristic features seen on SWI and T2 sequences.

Volumetric segmentation was performed on the MPRAGE sequence using the Freesurfer Version 6.0 image analysis suite (http://surfer.nmr.mgh.harvard.edu/).[6-17] Procedures for measuring cortical thickness have been validated against histological analysis[18] and manual measurements.[19,20] Freesurfer morphometric procedures have demonstrated good test-retest reliability across scanner manufacturers and across field strengths.[13,17]

The supratentorium is defined as the brain parenchyma located above the tentorium cerebelli and includes the bilateral cerebral hemispheres, basal ganglias, thalami, hypothalami, and the corpus callosum.

For the current analysis, 4 neuroradiologists (J.W., J.L., S.J., P.R.) measured the CSP and CV (CSPV) length (eFigure 1) by following the leaflets of the septum pellucidum posteriorly using the point that the leaflets contacted each other as the end of the CSP, then measuring the length on the sagittal plane anteriorly to posteriorly. If this length extended posterior to the anterior columns of the fornix, this was considered a CV. The transverse dimensions of the CSPs were measured at their greatest point on the coronal plane. The readers were blinded to whether the images belonged to a fighter or a control participant.

The same 4 neuroradiologists performed longitudinal follow-up in participants with reported CSP or CV to evaluate size increases between the first available scan and the last available scan. This analysis was performed using 3D software (AGFA) that aligned the brains to account for differences in head position. The readers were not blinded to the time order of the scans.

eAppendix 4. Statistics

In a post hoc analysis, the association between CSPV length and the 7 brain volumes of interest was assessed using a series of linear regression models. In each model, the brain volume was the outcome variable, CSPV length was the predictor of interest, and age, education, and total intracranial volume (to account for head size[21]) were included as covariates. *P* values were adjusted for multiple comparisons using Holm's step-down procedure, and a significance level of .05 was applied to the adjusted *P* values.

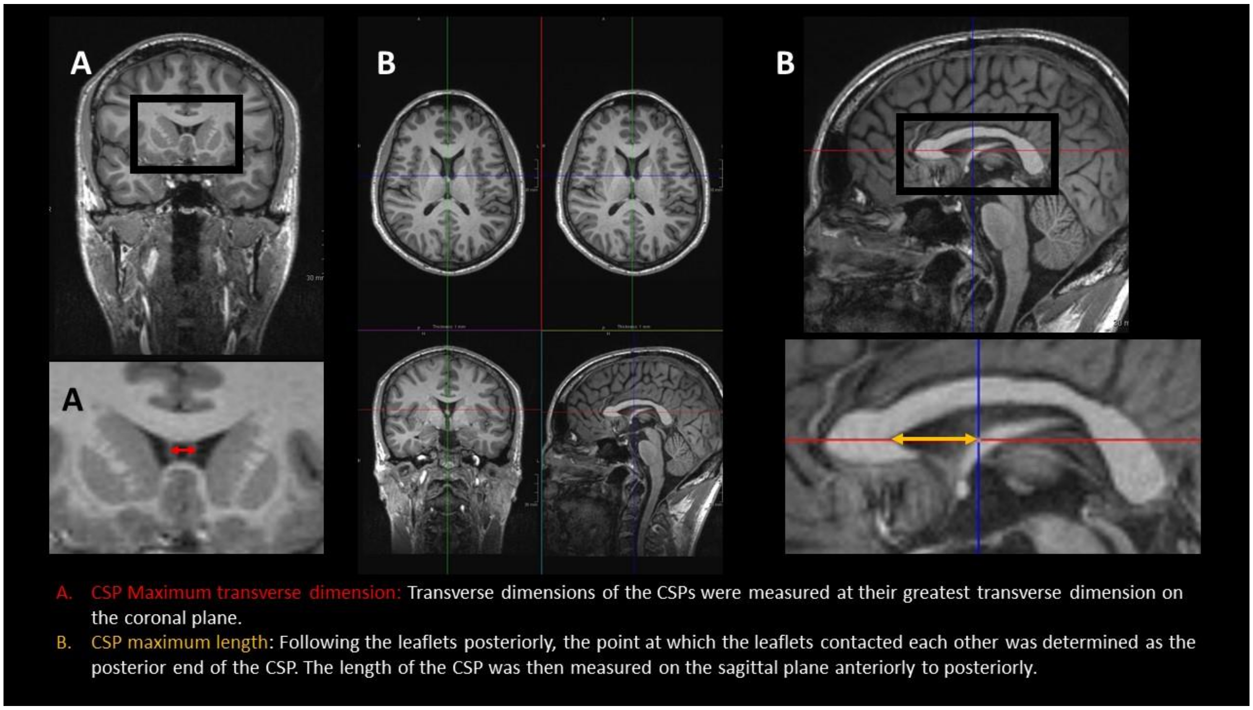
In a second post hoc analysis, the association between fighting status (fighter vs control) and a number of imaging characteristics, brain volumes, and cognitive scores was assessed using a series of regression models. Logistic regression was used in the case of binary variables (CSP and CV), and linear regression was used for the remaining variables. In each model, the imaging characteristic, brain volume, or cognitive score was the outcome variable, fighting status was the predictor of interest, and age, education, race, and ethnicity were included as covariates. *P* values were adjusted for multiple comparisons using Holm's step-down procedure, and a significance level of .05 was applied to the adjusted *P* values.

In a third post hoc analysis, the hypothesis that the association between brain volume and cognitive score would be different for fighters with versus fighters without CV was assessed by adding an interaction term (brain volume × CV status) to the model. The cognitive scores for psychomotor speed and processing speed were assessed separately.

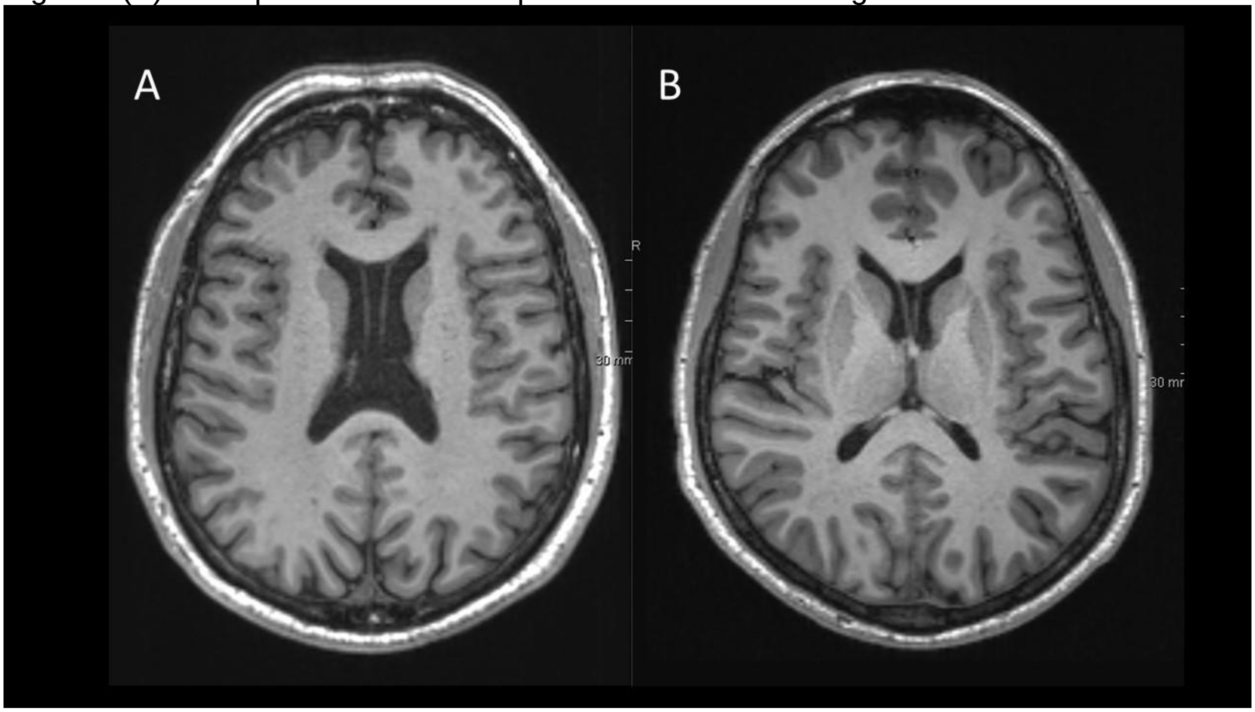
In a fourth post hoc analysis, the fighter exposure score was calculated as a combination of the number of professional fights and the mean number of professional fights per year.[22] Subsequently, the association between fighter exposure score and a number of imaging characteristics, brain volumes, and cognitive scores was assessed using a series of regression models. Logistic regression was used in the case of binary variables (CSP and CV), and linear regression was used for the remaining variables. In each model, the imaging characteristic, brain volume, or cognitive score was the outcome variable, fighter exposure score was the predictor of interest, and age, education, and total intracranial volume were included as covariates. *P* values were adjusted for multiple comparisons using Holm's step-down procedure, and a significance level of .05 was applied to the adjusted *P* values.

In a fifth post hoc analysis, follow-up data were analyzed. For the subset of fighters with follow-up data available, Spearman's correlation coefficient was calculated to quantify the association between (1) changes in CSPV length and changes in cognitive measures, (2) changes in CSPV length and changes in brain volumes, (3) changes in maximum transverse width of the CSP and changes in cognitive measures, and (4) changes in maximum transverse width of the CSP and changes in brain volumes.

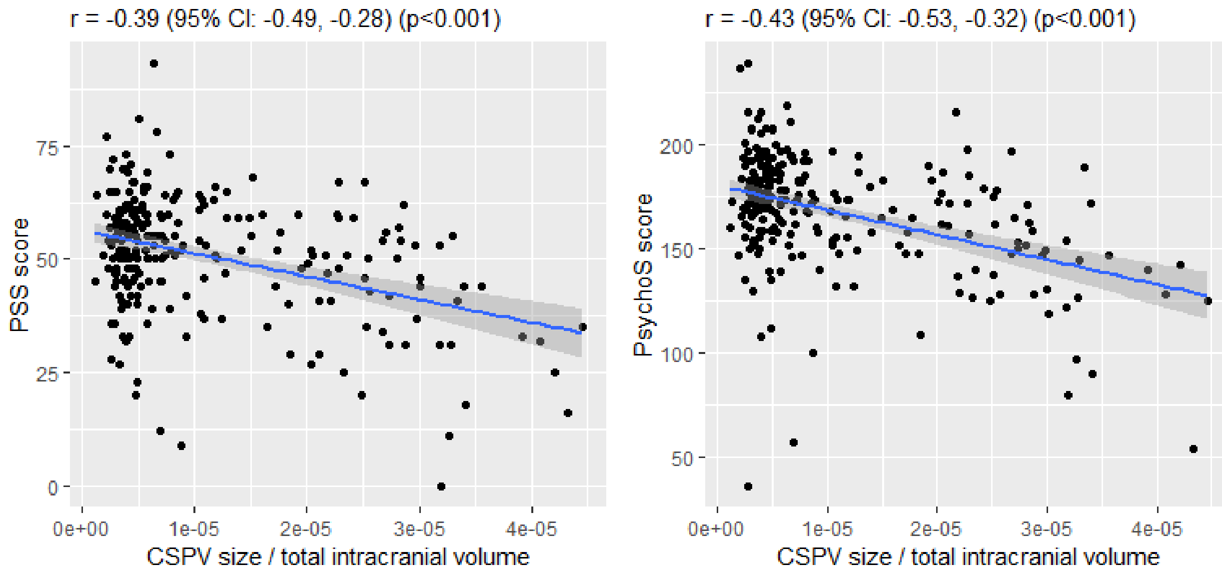
eFigure 1. (A) Measurement of the Cavum Septum Pellucidum (CSP) in the Maximum Transverse Dimension (B) Measurement of the CSP and Cavum Vergae (CV) in the Maximum Longitudinal Dimension



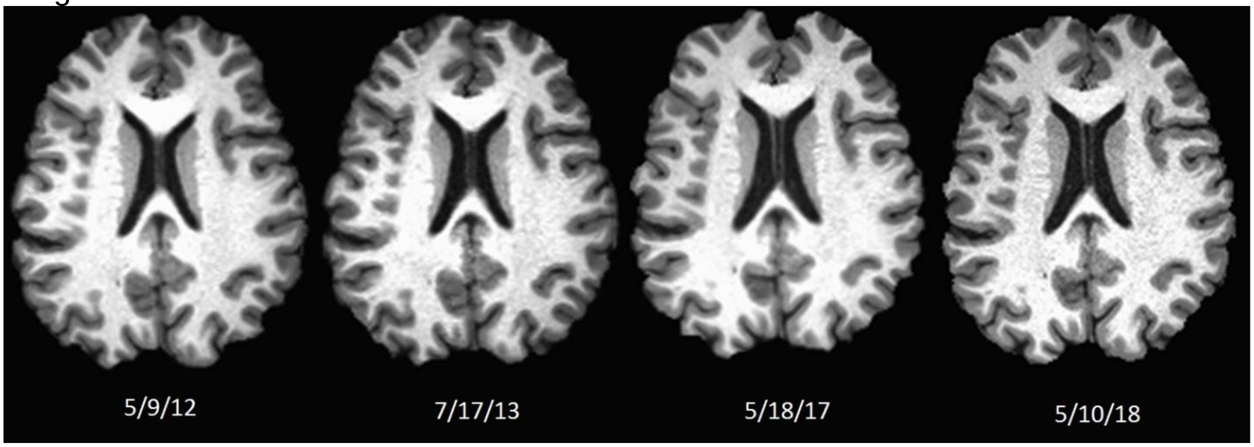
eFigure 2. (A) Example of a Cavum Septum Pellucidum and Cavum Vergae in a Fighter. (B) Example of a Cavum Septum Pellucidum in a Fighter



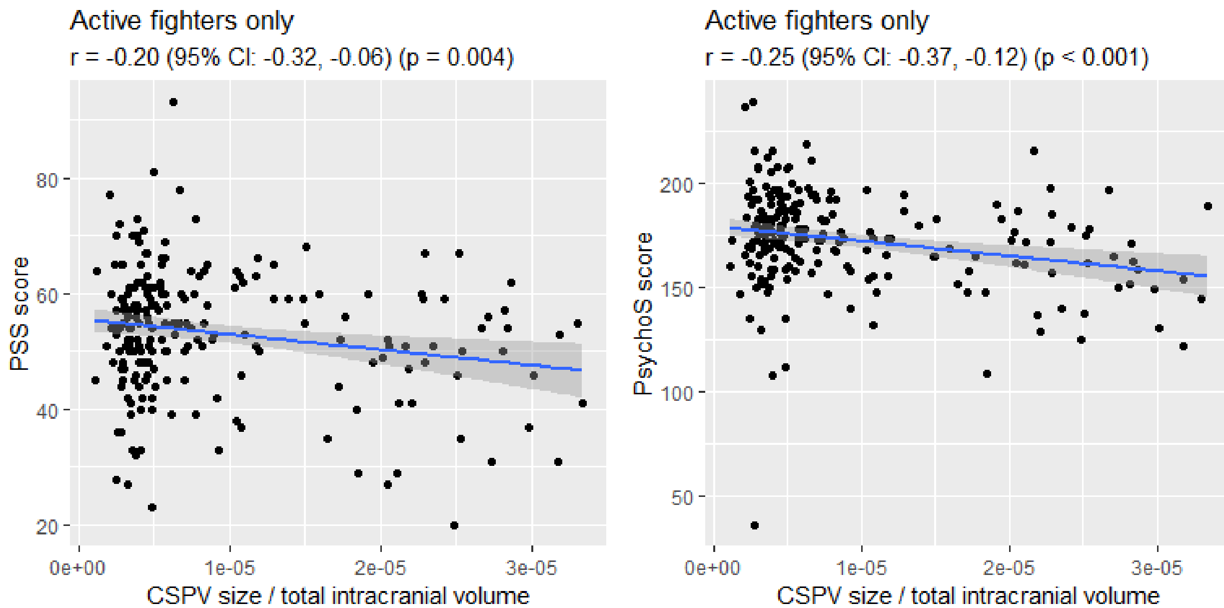
eFigure 3. Scatterplot of Cavum Septum Pellucidum and Cavum Vergae (CSPV) Length and Processing Speed (PSS) Score (Left) and Psychomotor Speed (PsychoS) Score (Right) Among 251 Fighters With CSPV Length Available



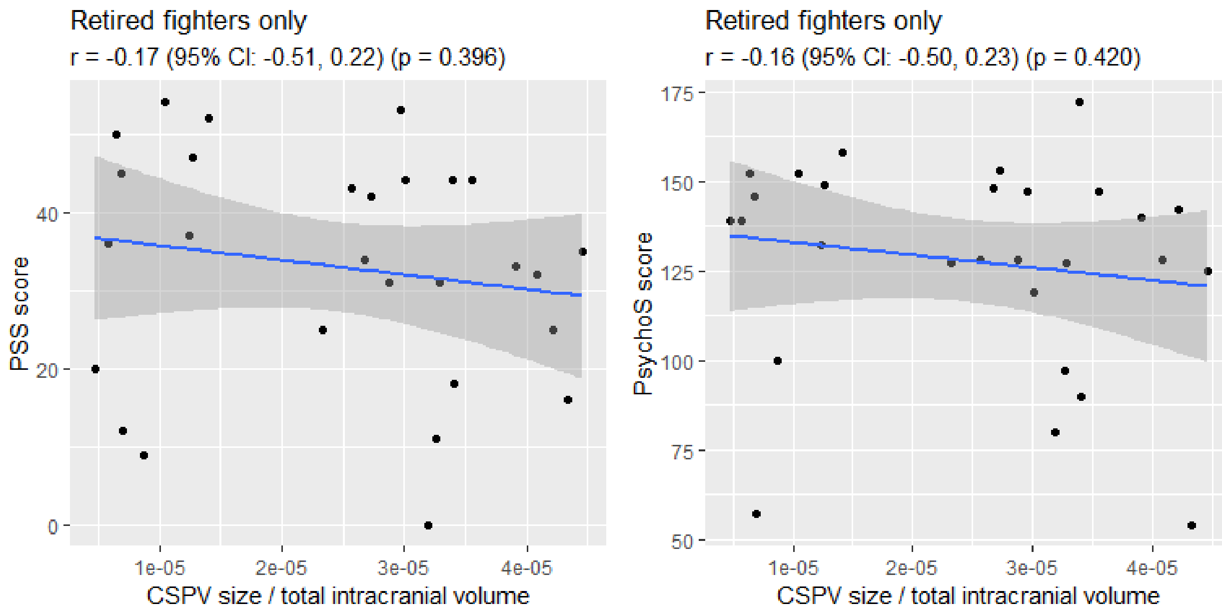
eFigure 4. Example of a Patient With Increased Cavum Septum Pellucidum/Cavum Vergae Over Time



eFigure 5. Scatterplot of Cavum Septum Pellucidum and Cavum Vergae (CSPV) Length and Processing Speed (PSS) Score (Left) and Psychomotor Speed (PsychoS) Score (Right) With Only Active Fighters



eFigure 6. Scatterplot of Cavum Septum Pellucidum and Cavum Vergae (CSPV) Length and Processing Speed (PSS) Score (Left) and Psychomotor Speed (PsychoS) Score (Right) With Only Retired Fighters



eTable 1. Characteristics of Study Participants

Characteristic	Entire Sample (n = 539)[a]	Fighters (n = 476)[a]	Controls (n = 63)[a]
Age	30 (8) [18, 72]	30 (8) [18, 72]	31 (10) [18, 58]
Years of education	14 (3) [2, 25]	13 (3) [2, 25]	14 (3) [9, 20]
Sex			
Male	497 (92%)	440 (92%)	57 (90%)
Female	42 (8%)	36 (8%)	6 (10%)
Race[b]			
White	232 (45%)	205 (46%)	27 (43%)
African American	134 (26%)	113 (25%)	21 (33%)
Asian	42 (8%)	34 (8%)	8 (13%)
Other	105 (20%)	99 (22%)	7 (11%)
Ethnicity[c]			
Hispanic	127 (28%)	123 (31%)	4 (7%)
Not Hispanic	326 (72%)	273 (69%)	53 (93%)
Fighting status			
Active	437 (92%)	437 (92%)	--
Retired	39 (8%)	39 (8%)	--
Type of fighter[d]			
100% boxing	181 (41%)	181 (41%)	--
70% boxing	6 (1%)	6 (1%)	--
100% mixed martial arts	196 (45%)	196 (45%)	--
70% mixed martial arts	10 (2%)	10 (2%)	--
100% Martial arts	28 (6%)	28 (6%)	--
70% Martial arts	2 (<1%)	2 (<1%)	--
<70% boxing, mixed martial arts, martial arts	15 (3%)	15 (3%)	--
No. of professional fights[e]	13 (17) [0,166]	13 (17) [0,166]	--
Mean no. of professional fights per year[f]	2.2 (2.2) [0, 20.2]	2.2 (2.2) [0, 20.2]	--
Total no. of fights[g]	49 (77) [0, 1006]	49 (77) [0, 1006]	--

[a]Data presented as mean (SD) or no. of participants (percent).
[b]Race was unknown for 26 participants.
[c]Ethnicity was unknown for 86 participants.
[d]Type of fighter was unknown for 38 fighters.
[e]No. of professional fights was unknown for 3 fighters.
[f]Mean no. of professional fights per year was unknown for 16 fighters.
[g]Total no. of fights was unknown for 25 fighters.

eTable 2A. Cognitive Scores Among Fighters With and Without CSP and CV[a]

Cognitive/Behavioral Measure	CSP				CV			
	Absent		Present		Absent		Present	
	No. of Fighters	Mean (SD)	No. of Fighters	Mean (SD)	No. of Fighters	Mean (SD)	No. of Fighters	Mean (SD)
PHQ9	227	2.5 (3.0)	243	3 (4.3)	403	2.5 (3.3)	67	4.3 (5.8)
ESS	227	5.3 (3.5)	243	5.8 (4.2)	404	5.4 (3.7)	66	6.1 (4.7)
Attention	221	9.8 (2.8)	233	9.7 (3.3)	389	9.7 (2.9)	65	10.1 (3.7)
Motor	221	14.8 (3.4)	233	14.8 (3.2)	389	14.8 (3.3)	65	14.5 (3.2)
Self-control	221	11.7 (3.4)	233	12 (3.8)	389	11.8 (3.3)	65	12.6 (4.8)
Cognitive complexity	221	11.8 (2.4)	233	11.9 (2.5)	389	11.8 (2.3)	65	12.4 (2.8)
Perseverance	221	6.9 (2.0)	233	6.7 (1.9)	389	6.8 (1.9)	65	6.8 (2.1)
Cognitive instability	221	5.2 (1.7)	233	5.2 (1.7)	389	5.2 (1.7)	65	5.2 (2.0)
Total impulsivity	221	60.2 (10.3)	233	60.4 (11.3)	389	60.1 (10.1)	65	61.6 (14.4)
Verbal memory	225	51.3 (5.0)	240	51 (5.1)	401	51.3 (4.9)	64	50.4 (5.7)
Processing speed	228	53.4 (11.4)	246	50.9 (13.1)	407	53.4 (11.6)	67	44.4 (14.1)
Psychomotor speed	228	175 (20.5)	246	168 (28)	407	174 (23.1)	67	153 (28.6)
Reaction time	228	698 (97.8)	243	718 (120)	406	699 (98.7)	65	761 (156)

Abbreviations: CSP, cavum septum pellucidum; CV, cavum vergae; ESS, Epworth Sleepiness Scale; PHQ9, Patient Health Questionnaire-9.
[a]Analysis not adjusted for any covariates.

eTable 2B. Cognitive Scores Among Fighters With and Without WMC and CMH[a]

Cognitive/Behavioral Measure	WMC				CMH			
	Absent		Present		Absent		Present	
	No. of Fighters	Mean (SD)	No. of Fighters	Mean (SD)	No. of Fighters	Mean (SD)	No. of Fighters	Mean (SD)
PHQ9	357	2.4 (3.2)	110	4.0 (5.1)	446	2.7 (3.7)	20	2.6 (3.7)
ESS	357	5.4 (3.6)	110	5.8 (4.5)	446	5.6 (3.9)	20	4.0 (2.5)
Attention	345	9.6 (3.0)	106	10.2 (3.2)	430	9.8 (3.1)	20	9.4 (2.5)
Motor	345	14.6 (3.2)	106	15.4 (3.5)	430	14.8 (3.2)	20	14.6 (4.4)
Self-control	345	11.6 (3.4)	106	12.9 (4.1)	430	11.9 (3.5)	20	11.8 (4.3)
Cognitive complexity	345	11.7 (2.4)	106	12.6 (2.4)	430	11.9 (2.4)	20	11.3 (2.8)
Perseverance	345	6.8 (1.9)	106	6.8 (2.1)	430	6.8 (1.9)	20	6.3 (1.7)
Cognitive instability	345	5.2 (1.7)	106	5.3 (1.8)	430	5.2 (1.7)	20	4.8 (1.5)
Total impulsivity	345	59.5 (10.4)	106	63.2 (11.6)	430	60.4 (10.7)	20	58.4 (11.7)
Verbal memory	352	51.5 (4.9)	110	50.2 (5.4)	440	51.2 (5.0)	21	52.0 (5.3)
Processing speed	361	52.8 (12)	110	49.9 (13.4)	449	52.2 (12.4)	21	50.3 (12.3)
Psychomotor speed	361	172 (22.8)	110	167 (30.6)	449	171 (24.9)	21	169 (26.0)
Reaction time	358	701 (107)	110	731 (117)	446	707 (110)	21	726 (119)

Abbreviations: CMH, cerebral microhemmorrhages; ESS, Epworth Sleepiness Scale; PHQ9, Patient Health Questionnaire-9; WMC, white matter changes.
[a]Analysis not adjusted for any covariates.

eTable 3. Change in Psychomotor Speed With Increase in Various Brain Volumes Without and With CV[a,b]

	Estimated change in psychomotor speed with each 100 mm^3 increase in brain volume	
Location	Fighters without CV	Fighters with CV
Thalamus	0.27	0.53
Caudate	-0.01	0.56
Putamen	-0.07	0.54
Hippocampus	0.06	0.99
Amygdala	-0.03	2.15

Abbreviations: CV, cavum vergae.
[a]All associations adjusted for age and education

eTable 4. Association Between Fighter Exposure Score and Various Imaging Characteristics, Brain Volumes, and Cognitive Scores

Variable	**No. of Observations**	**Estimate (95% CI)[a,b]**	***P* Value[c]**
CSP	429	1.08 (0.93, 1.24)	1.000
CSPV length	235	0.39 (-0.81, 1.6)	1.000
Mean transverse width of CSP	235	0.01 (-0.11, 0.12)	1.000
CV	429	1.10 (0.89, 1.36)	1.000
Supratentorial volume	429	-2960.43 (-6156.36, 235.5)	.540
Thalamic volume	429	-110.35 (-189.9, -30.8)	.088
Corpus callosum volume	429	-28.49 (-60.17, 3.2)	.540
Caudate volume	429	-76.13 (-130.99, -21.27)	.088
Putamen volume	429	-68.91 (-142.61, 4.79)	.540
Hippocampal volume	429	-29.70 (-75.3, 15.9)	1.000
Amygdala volume	429	-24.17 (-48.69, 0.36)	.487
Processing speed	427	-0.78 (-1.5, -0.06)	.347
Psychomotor speed	427	-2.02 (-3.56, -0.47)	.121

Abbreviations: CSP, cavum septum pellucidum; CSPV, cavum septum pellucidum and cavum vergae; CV, cavum vergae.
[a]Estimates are odds ratios for binary variables (CSP and CV) and slopes for remaining variables.
[b]All associations adjusted for age, education, and total intracranial volume.
[c]*P* values adjusted for multiple comparisons using Holm's step-down method.

eTable 5. Correlation Between Changes in CSPV Length and Changes in Various Cognitive/Behavioral Measures

Cognitive/Behavioral Measure	No. of Observations	Correlation With Change in CSPV Length (95% CI)[a]	*P* Value	Adjusted *P* Value
PHQ9	123	–0.16 (–0.33 to 0.02)	.071	.923
ESS	78	0.02 (–0.22 to 0.25)	.853	>.99
Attention	116	–0.02 (–0.21 to 0.15)	.840	>.99
Motor	116	–0.06 (–0.24 to 0.11)	.552	>.99
Self-control	116	0.06 (–0.13 to 0.24)	.549	>.99
Cognitive complexity	116	–0.10 (–0.27 to 0.09)	.310	>.99
Perseverance	116	0.04 (–0.16 to 0.22)	.705	>.99
Cognitive instability	116	–0.03 (–0.23 to 0.16)	.747	>.99
Total impulsivity	116	–0.05 (–0.23 to 0.13)	.612	>.99
Verbal memory	122	–0.13 (–0.29 to 0.05)	.168	>.99
Processing speed	125	0.06 (–0.11 to 0.24)	.472	>.99
Psychomotor speed	125	0.01 (–0.16 to 0.18)	.873	>.99
Reaction time	124	–0.08 (–0.26 to 0.11)	.353	>.99

Abbreviations: CSPV, cavum septum pellucidum and cavum vergae; ESS, Epworth Sleepiness Scale; PHQ9, Patient Health Questionnaire-9.

[a]Correlation is characterized using Spearman's correlation coefficient.

eTable 6. Correlation Between Changes in CSPV Length and Changes in Various Brain Volumes

Volume	No. of Observations	Correlation With Change in CSPV Length (95% CI)[a]	*P* Value	Adjusted *P* Value
Thalamus	113	–0.04 (–0.22 to 0.13)	.636	>.99
Corpus callosum	113	0.08 (–0.11 to 0.27)	.394	>.99
Caudate	113	–0.10 (–0.30 to 0.09)	.276	>.99
Putamen	113	–0.22 (–0.39 to –0.05)	.017	.119
Hippocampus	113	0.07 (–0.13 to 0.26)	.469	>.99
Amygdala	113	0.04 (–0.13 to 0.22)	.705	>.99
Supratentorial volume	113	–0.12 (–0.29 to 0.07)	.199	>.99

Abbreviation: CSPV, cavum septum pellucidum and cavum vergae.
[a]Correlation is characterized using Spearman's correlation coefficient.

eTable 7. Characteristics of Active Versus Retired Fighters

	Active Fighters		Retired Fighters		***P* Value**
Variable	#	summary	#	summary	
Age	437	28 (6) [18, 32]	39	47 (11) [21, 53]	**<.001**
Male	437	402 (92%)	39	38 (97%)	.344
Years of education	437	13 (3) [2, 20]	39	13 (4) [3, 25]	.550
Fight Exposure Score	422		38		**<.001**
0		98 (23%)		1 (3%)	
1		64 (15%)		3 (8%)	
2		148 (35%)		4 (11%)	
3		1 (<1%)		0 (0%)	
4		111 (26%)		30 (79%)	
Race	413		37		.086
White		191 (46%)		14 (38%)	
African American		99 (24%)		14 (38%)	
Asian		34 (8%)		0 (0%)	
Other		89 (22%)		9 (24%)	
Ethnicity	359		37		.853
Hispanic		111 (31%)		12 (32%)	
Not Hispanic		248 (69%)		25 (68%)	

[a]Summaries presented as mean (standard deviation) [range] or count (percent).

eTable 8. Comparison of Imaging and Cognitive Variables in Active Fighters and Controls

Variable	Active Fighters		Controls		*P* Value[b]
	Total No. of Participants	**Observed Value[a]**	**Total No. of Participants**	**Observed Value[a]**	
Presence of CSP	437	217 (50%)	63	11 (17%)	**<.001**
Presence of CV	437	47 (11%)	63	0 (0%)	**.017**
CSPV length, mm	221	14 (12)	11	9 (5)	1.000
Mean transverse width of CSP, mm	221	3 (1)	11	3 (1)	1.000
Supratentorial volume, mm^3	407	1077055 (96947)	62	1054332 (106459)	.405
Thalamic volume, mm^3	407	13956 (1484)	62	14451 (1465)	.177
Corpus callosum volume, mm^3	407	3089 (493)	62	3490 (553)	**<.001**
Caudate volume, mm^3	407	7748 (943)	62	7347 (963)	**.049**
Putamen volume, mm^3	407	12082 (1268)	62	11059 (1427)	**<.001**
Hippocampal volume, mm^3	407	8034 (724)	62	8162 (732)	1.000
Amygdala volume, mm^3	407	3491 (395)	62	3531 (369)	1.000
Processing speed	435	54 (11)	63	61 (16)	**<.001**
Psychomotor speed	435	174 (22)	63	191 (60)	**.001**

Abbreviations: CSP, cavum septum pellucidum; CSPV, cavum septum pellucidum and cavum vergae; CV, cavum vergae.
[a]Data presented as mean (SD) or no. of participants (percent).
[b]*P* values adjusted for multiple comparisons using Holm's step-down method.

eTable 9. Estimated Mean Differences for Various Brain Volumes Among Active Fighters With and Without CSP and CV

Location	Adjusted Mean Difference in Brain Volume, mm^3			
	CSP Present vs Absent (95% CI)[a,b]	*P* Value[c]	CV Present vs Absent (95% CI)[a,b]	*P* Value[c]
Supratentorium	25818 (4416, 47220)	.128	-14807 (-49944, 20331)	.446
Thalamus	-11 (-349, 327)	1.000	-572 (-1118, -26)	.241
Corpus callosum	43 (-68, 154)	1.000	-185 (-365, -5)	.241
Caudate	-94 (-312, 123)	1.000	-403 (-755, -52)	.173
Putamen	11 (-262, 284)	1.000	-359 (-802, 84)	.446
Hippocampus	74 (-94, 242)	1.000	-207 (-479, 66)	.446
Amygdala	48 (-46, 142)	1.000	-113 (-265, 40)	.446

Abbreviations: CSP, cavum septum pellucidum; CV, cavum vergae.
[a]Positive values indicate higher volumes when the imaging characteristic is present; negative values indicate higher volumes when the imaging characteristic is absent.
[b]Estimates adjusted for age, education, race, and ethnicity.
[c]*P* values adjusted for multiple comparisons using Holm's step-down method.

eTable 10. Estimated Change in Mean Brain Volumes With Each 1-mm Enlargement in CSPV Length in Active Fighters

Location	**Estimated Change in Brain Volume With Each 1-mm Increase in CSPV Length, mm^3 (95% CI)[a,b]**	***P* Value[c]**
Supratentorium	-1104 (-1746, -461)	**.006**
Thalamus	-25 (-40, -10)	**.006**
Corpus callosum	-12 (-18, -6)	**.000**
Caudate	-16 (-26, -6)	**.012**
Putamen	-14 (-28, 0)	.096
Hippocampus	-8 (-17, 1)	.096
Amygdala	-6 (-11, -1)	**.033**

Abbreviation: CSPV, cavum septum pellucidum and cavum vergae.
[a]Positive values indicate higher volumes when CSPV length increases; negative values indicate lower volumes when CSPV length increases.
[b]Estimates adjusted for age, education, race, ethnicity, and total intracranial volume.
[c]*P* values adjusted for multiple comparisons using Holm's step-down method

eTable 11. Comparison of Imaging and Cognitive Variables in Retired Fighters and Controls

	Retired Fighters		Controls		
Variable	**Total No. of Participants**	**Observed Value[a]**	**Total No. of Participants**	**Observed Value[a]**	***P* Value[b]**
Presence of CSP	39	30 (77%)	63	11 (17%)	**.003**
Presence of CV	39	20 (51%)	63	0 (0%)	**<.001**
CSPV length, mm	30	35 (17)	11	9 (5)	**.018**
Mean transverse width of CSP, mm	30	5 (2)	11	3 (1)	.222
Supratentorial volume, mm^3	34	937455 (112095)	62	1054332 (106459)	.214
Thalamic volume, mm^3	34	11136 (1883)	62	14451 (1465)	**<.001**
Corpus callosum volume, mm^3	34	2409 (682)	62	3490 (553)	**.001**
Caudate volume, mm^3	34	6591 (1183)	62	7347 (963)	.866
Putamen volume, mm^3	34	9950 (1604)	62	11059 (1427)	.866
Hippocampal volume, mm^3	34	6852 (929)	62	8162 (732)	**.001**
Amygdala volume, mm^3	34	2834 (512)	62	3531 (369)	**<.001**
Processing speed	39	36 (14)	63	61 (16)	**.006**
Psychomotor speed	39	135 (28)	63	191 (60)	**.012**

Abbreviations: CSP, cavum septum pellucidum; CSPV, cavum septum pellucidum and cavum vergae; CV, cavum vergae.
[a]Data presented as mean (SD) or no. of participants (percent).
[b]*P* values adjusted for multiple comparisons using Holm's step-down method.

eTable 12. Estimated Mean Differences for Various Brain Volumes Among Retired Fighters With and Without CSP and CV

Location	Adjusted Mean Difference in Brain Volume, mm^3			
	CSP Present vs Absent (95% CI)[a,b]	*P* Value[c]	CV Present vs Absent (95% CI)[a,b]	*P* Value[c]
Supratentorium	-31936 (-145444, 81572)	1.000	-58786 (-131067, 13495)	.636
Thalamus	-682 (-2648, 1284)	1.000	-341 (-1665, 983)	1.000
Corpus callosum	-158 (-1070, 754)	1.000	-245 (-849, 359)	1.000
Caudate	-803 (-2145, 538)	1.000	-394 (-1306, 519)	1.000
Putamen	-1073 (-3039, 892)	1.000	-1165 (-2421, 91)	.472
Hippocampus	-726 (-1842, 391)	1.000	-551 (-1291, 189)	.685
Amygdala	-199 (-834, 436)	1.000	-264 (-678, 150)	.798

Abbreviations: CSP, cavum septum pellucidum; CV, cavum vergae.
[a]Positive values indicate higher volumes when the imaging characteristic is present; negative values indicate higher volumes when the imaging characteristic is absent.
[b]Estimates adjusted for age, education, race, and ethnicity.
[c]*P* values adjusted for multiple comparisons using Holm's step-down method.

eTable 13. Estimated Change in Mean Brain Volumes With Each 1-mm Enlargement in CSPV Length in Retired Fighters

Location	Estimated Change in Brain Volume With Each 1-mm Increase in CSPV Length, mm^3 (95% CI)[a,b]	*P* Value[c]
Supratentorium	-954 (-2932, 1024)	1.000
Thalamus	-10 (-50, 30)	1.000
Corpus callosum	-7 (-26, 12)	1.000
Caudate	-2 (-29, 25)	1.000
Putamen	-34 (-73, 5)	.588
Hippocampus	-12 (-35, 11)	1.000
Amygdala	-5 (-17, 8)	1.000

Abbreviation: CSPV, cavum septum pellucidum and cavum vergae.
[a]Positive values indicate higher volumes when CSPV length increases; negative values indicate lower volumes when CSPV length increases.
[b]Estimates adjusted for age, education, race, ethnicity, and total intracranial volume.
[c]*P* values adjusted for multiple comparisons using Holm's step-down method

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