Supplementary Materials

Materials and Methods

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Sample size, inclusion and exclusion criteria

Sample size was calculated with GPower 3.1.9.7 program. We specified a two-sided significance level set at 0.05, with a power of 0.80, and with the objective of reaching an effect size of Cohen's d = 0.6, allocation ratio 2:1. With these parameters stipulated the study would require 68 patients and 34 controls. We recruited 86 patients and 36 controls in order to consider drop-outs or exclusions. Final sample size of the present study is 84 PCS and 33 controls.

Inclusion criteria for the PCS group were: 1) Diagnosis of COVID-19 confirmed by RT-PCR at least three months before the inclusion in the study; 2) Cognitive complaints temporally related to the SARS-CoV-2 infection. Patients were excluded if they presented with other neurological, or psychiatric disorders that could affect the study outcomes. Specifically, exclusion criteria included: 1) Any cognitive complaint before COVID-19, asked to the patient during the clinical interview; 2) History of stroke, traumatic brain injury, or any neurological disorder potentially associated with cognitive impairment; 3) Active psychiatric disorder or previous psychiatric disease with a potential cognitive effect (e.g. schizophrenia); 4) History of abuse of alcohol or other toxics; 5) Drugs or uncontrolled medical conditions associated with cognitive impairment at the moment of the assessment 6) Sensory disorder potentially biasing cognitive assessments; 7) Deep white matter cerebral small vessel disease (Fazekas grade 2 or higher). Exclusion criteria for HC were: 1) History of SARS-CoV-2 infection evaluated trough a serological analysis; 2) Presence of cognitive impairment or cognitive complaints; 3) History of stroke, traumatic brain injury, or any neurological disorder potentially associated with cognitive impairment; 4) Active psychiatric disorder or previous psychiatric disease with a potential cognitive effect (e.g. schizophrenia); 5) History of abuse of alcohol or other toxics; 6) Drugs or uncontrolled medical conditions associated with cognitive impairment

at the moment of the assessment 7) Sensory disorder potentially biasing cognitive assessments; 8) Deep white matter cerebral small vessel disease (Fazekas grade 2 or higher).

Eighty-six PCS patients and 36 HC were enrolled in the study. After the enrollment, one patient was excluded due to absence of T2 acquisition sequence, and two HC were excluded due to absence of diffusion-weighted images acquisition. Additionally, one PCS patient and one HC were excluded after quality check of hippocampal segmentation. Therefore, final sample size was 84 PCS and 33 HC.

Additionally, blood biomarker comparison was performed with an additional HC group (n=X).

Neuropsychological and clinical assessment

Neuropsychological tests included were: Forward and Backward Digit Span, Corsi Block-Tapping Test (forward and backward), Symbol Digit Modalities Test (SDMT), Free and Cued Selective Reminding Test (FCSRT), Rey-Osterrieth Complex Figure (ROCF) (copy and recall at 3, 30 min, and recognition), verbal fluency (animals and words beginning with “P”, “R”, and “M” in one minute each one), Stroop Word-Color Interference Test, Boston Naming Test (BNT), Judgment Line Orientation (JLO), and the Visual Object and Space Perception Battery (VOSP). These tests were validated and normative data are available in our country, adjusted by age and education level (60, 61). Impairment was set at two cut-off scores, first, at the scaled-score of five or less, which is equivalent to a percentile of ≤ 5 or z-score ≤ 1.65, and at the scaled-score of seven or less, which is equivalent to a percentile of ≤ 16 or z-score ≤ 1.

Clinical evaluation included the Modified Fatigue Impact Scale (MFIS) for fatigue assessment (62), Beck Depression Inventory-II (63), Brief Smell Identification Test (BSIT) (64) and the Pittsburgh Sleep Quality Index (PSQI) (65) were also administered

to the PCS patients. The following cut-offs were used according to the previous literature: BSIT ≤ 8 was categorized as having abnormal olfaction; BDI-II ≥ 19 was regarded as moderate or severe depression (66); PSQI >5 defined poor sleep quality and MFIS ≥ 38 was considered as having fatigue (67).

Neuroimaging acquisition parameters

Patients were scanned using a 3.0T Magnet (GE Signa Architect) and a 48-channel head coil. 3D T1-weighted images were acquired in a Sagittal MPRAGE sequence with the following parameters: number of slices = 200, slice thickness = 1 mm, field of view 256 mm, matrix = 256x256, flip angle = 8, preparation time = 974 ms, recovery time = 700 ms, TR = 7.7 ms, TE = 3.1 ms, NEX= 1, voxel size = 1 x 1 x 1 mm, acquisition time = 9:27.

A dedicated high resolution in-plane T2 weighted (0.34x0.34mm) perpendicular to the hippocampal axis was also acquired in order to adequate the output, with the following parameters: number of slices= 32, slice thickness= 2 mm, field of view 175 mm, matrix=448x448, TR=5280 ms, TE=80 ms, echo train length=30, NEX= 2, acquisition time=4:12.

Diffusion-weighted images were acquired in axial multishell diffusion 1 shot echo-planar sequence, with 3 b values (500,1000, 2000), and 125 diffusion directions, and the following parameters: number of slices = 64, slice thickness = 2.2 mm, field of view 256 mm, matrix = 116x166, TR = 6780 ms, TE = 3.1 ms, NEX = 1, voxel size = 2 x 2 x 2.2 mm, acquisition time = 14:35. An additional opposing gradients sequence was acquired, for geometrical distortions correction purpose.

The resting-state fMRI data were obtained in an axial orientation using a sequence sensitive to blood oxygen level-dependent (BOLD) contrast, and multi-slice gradient

echo EPI sequence (TR = 3000 ms, TE = 30 ms, matrix size = 64 x 64, flip angle = 90°, FOV = 220x220mm, slice thickness = 3.4 mm, no gap, 205 volumes, 48 slices, voxel size = 3.4 x 3.4 x 3.4 mm, acquisition time = 10′15″).

Finally, arterial spin labeling (ASL) was acquired with the following parameters: number of slices = 36, slice thickness = 4 mm, field of view = 240 mm, resolution = 4x3.73x3.73 mm, flip angle = 111, labeling time = 1.5 s, post-labeling delay = 2025 ms, TR = 4854 ms, TE = 53.52 ms, NEX = 3, voxel size = 1.87 x 1.87 x 4 mm, acquisition time = 4:25. Head holders and restraints were used to prevent motion artifacts.

Blood biomarker measurement

For the detection of biomarkers we performed sensitive ELISA techniques using the following commercial kits: GFAP (sensitive indicators for astrocyte activation/injury (21), REF Human GFAP ELISA Kit - 96T E-EL-H6093, Elabscience), MOG (oligodendrocyte structural protein related to myelin processes (22), REF Human Myelin-oligodendrocyte glycoprotein, ELISA Kit - MBS928110-96, Mybiosorse), CCL11/ Eatoxin (cytokine ion involved in acute phases of inflammation and described as an inhibitor of hippocampal neurogenesis (51), REF Human Eosinophil Chemotactic Factor ELISA Kit - 96T - E-EL-H0025-96T, Elabscience), and NfL (neurofilament light chain, closely associated with neuraxonal damage and neurodegeneration (81), REF OKCD01380 Aviva Systems Biolog).

Samples were collected in blood sample collection tubes with yellow cap or EDTA-treated with purple cap tubes. Cellular phase (erythrocytes, platelets, and leukocytes) was isolated by centrifugation for 15 min at 2,500 × g, obtaining the serum or plasma, and the samples were stored at –80◦C.

Brain tissue autopsy: Procedure and Preparation and Storing of Biological Material

Selection and study of patients and controls

Patients and controls (or their legal guardians) signed an informed consent for tissue donation. In order to carry out autopsies, the legally established authorizations regarding donations for research are required. The handling of patient data is in compliance with Regulation (EU) 2016/679 of the European Parliament and of the Council, of April 27, 2016, regarding the protection of natural persons and Organic Law 3/2018. Protection of Personal Data and guarantee of digital rights, in force since December 7, 2018. Patient data is encrypted and archived with protection so that only the responsible researcher has access to it. Processing was carried out exclusively by authorized individuals. The project was carried out according to the Helsinki guidelines (Recommendations Guiding Physicians in Biomedical Research Involving Human Subjects, Helsinki 1964, amended during the 52nd General Assembly of the World Medical Association, Edinburgh, Scotland, October 2000).

Autopsy Procedure and Preparation and Storing of Biological Material

Autopsies were performed within 4-8 hours after death following our hospital's standard protocol and in compliance with Spanish regulations for this procedure. We followed the standard method: opening the cranial cavity and severing the upper end of the spinal cord at the foramen magnum. To separate the hemispheres, we cut right along the midline of the corpus callosum and prepared them for later sectioning. Tissue samples were fixed in 10% buffered formalin [phosphate-buffered saline (PBS); 0.1M, pH 7.35]. The hemisphere allocated to histological and immunohistochemical analyses was sectioned into coronal slices (maximum slice thickness =1 cm), which were placed on a flat surface in order from the frontal pole to the occipital pole. From the patients we proceed to extract

a section of the brain that contains the hippocampus, carving and dissecting that anatomical area for subsequent histological analysis or IHC. The nervous system analysis included weighing the brain, examining its macroscopic morphology, and conducting a microscopic study, using conventional techniques.

Immunohistochemical Study

The tissues were embedded in paraffin under the usual procedure of the pathological anatomy service of the Hospital Clinico San Carlos. Tissue was sectioned into 6-µm slices using a microtome (Leica). Slices were deparaffinized and thoroughly washed with PBS 0.1M. Epitopes were unmasked in a 10-mM sodium citrate buffer with a pH of 6 at 96°C for 30 min. For autofluorescence blocking we used the TrueBlack® solution at a 1:100 dilution for 2 minutes (Biotium 23014). Following this, all samples were incubated in a blocking solution (PBS, 0.2 Triton X-100, 10% normal goat serum) for 1 h. After that, tissues were incubated in primary antibodies diluted in PBS for 72 h, 4°C, for CCL11 Eotaxin (Rabbit Proteintech 11786-1-AP), MOG (Rabbit ABCAM ab32760), and Astrocytes (GFAP, Chicken ThermoFisher-Invitrogen PA1-10004). After incubation with primary antibodies, sections were washed with PBS and incubated in the appropriate Alexa-Fluor secondary antibody 24 h 4°C, and counterstained with DAPI at a 1:3000 dilution in PBS. After thoroughly washing the sections, they were mounted in Fluorsave reagent with DAPI (Chemicon) and observed in an Olympus confocal microscope AF1000. The area analyzed was the subgranular zone of the hippocampus. For the quantitative analysis of GFAP, MOG and CCL11, two fields were used per control individual or COVID-19, acquiring the images with the 20x objective.

Supplementary Table S1: Hippocampal subfields volume in PCS and HC

	PCS (n=84)	HC (n=33)	F	*p* value*	Partial Eta Squared
HEAD					
CA1_head_BIL	510.749673 (55.773157)	539.422936 (90.976742)	12.421	<0.001*	0.248
CA1_head_L	502.939629 (61.385389)	530.443730 (95.863270)	9.587	<0.001*	0.203
CA1_head_R	518.559717 (58.768289)	548.402142 (89.817115)	12.687	<0.001*	0.252
CA3_head_BIL	123.440088 (17.771212)	128.596770 (25.470659)	12.745	<0.001*	0.253
CA3_head_L	116.000698 (19.217685)	122.880943 (24.125524)	10.605	<0.001*	0.220
CA3_head_R	130.879477 (18.781115)	134.312598 (28.046604)	12.095	<0.001*	0.243
CA4_head_BIL	121.607753 (15.515067)	128.062385 (23.234114)	15.499	<0.001*	0.292
CA4_head_L	117.362385 (16.472607)	124.341821 (23.284040)	12.708	<0.001*	0.252
CA4_head_R	125.853122 (16.165673)	131.782950 (24.201554)	15.465	<0.001*	0.291
GC_ML_DG_head_BIL	150.709392 (20.880172)	159.103594 (31.892451)	16.265	<0.001*	0.302
GC_ML_DG_head_L	145.465519 (21.571612)	154.682814 (31.966454)	13.096	<0.001*	0.258
GC_ML_DG_head_R	155.953264 (22.359348)	163.524375 (33.093871)	16.556	<0.001*	0.305
HATA_BIL	52.670555 (8.712737)	54.819520 (12.234785)	13.291	<0.001*	0.261
HATA_L	51.592696 (9.292746)	53.613234 (12.985355)	13.610	<0.001*	0.265
HATA_R	53.748415 (9.453934)	56.025807 (12.470833)	9.512	<0.001*	0.202
Molecular layer HP Head BIL	284.952545 (34.716272)	289.736958 (55.360170)	7.198	<0.001*	0.160
Molecular layer HP Head L	291.085570 (40.853901)	293.769675 (59.417758)	6.403	<0.001*	0.145
Molecular layer HP Head R	278.819520 (34.696051)	285.704241 (54.792986)	6.180	0.001*	0.141
Parasubiculum BIL	62.045830 (11.098140)	62.213310 (12.320537)	2.176	0.095	0.055
Parasubiculum L	63.264514 (12.717558)	61.777267 (13.218211)	2.813	0.043	0.069
Parasubiculum R	60.827145 (13.152610)	62.649354 (14.370380)	1.018	0.387	0.026
Subiculum Head BIL	160.034283 (19.910129)	166.075364 (28.457348)	4.129	0.008*	0.099
Subiculum Head L	164.482860 (24.144602)	168.244589 (33.647728)	3.747	0.013*	0.090
Subiculum Head R	155.585706 (19.992935)	163.906139 (26.585036)	3.624	0.015*	0.088
Presubiculum Head BIL	112.490496 (11.708937)	115.571114 (18.057144)	5.142	0.002*	0.120
Presubiculum Head L	112.292706 (13.429865)	114.120816 (19.475523)	3.900	0.011*	0.094
Presubiculum Head R	112.688286 (12.433817)	117.021411 (18.655976)	5.023	0.003*	0.118

BODY					
CA1_body_BIL	118.449550 (18.354178)	122.614794 (22.217726)	7.111	<0.001*	0.159
CA1_body_L	112.811627 (23.058742	119.538952 (22.830618)	5.237	0.002*	0.122
CA1_body_R	124.087474 (17.617792)	125.690636 (25.627215)	7.162	<0.001*	0.160
fimbria_BIL	78.719907 (21.231873)	84.081470 28.190770)	23.350	<0.001*	0.383
fimbria_L	80.026895 (25.010959)	82.441250 (30.297176)	15.602	<0.001*	0.293
fimbria_R	77.412920 (22.101883)	85.721690 (27.732282)	22.802	<0.001*	0.377
Molecular layer HP Body BIL	215.747380 (23.610162)	220.871699 (32.172505)	4.116	0.008*	0.099
Molecular layer HP Body L	203.729257 (24.817263)	210.428981 (29.936871)	2.661	0.052	0.066
Molecular layer HP Body R	227.765502 (27.501663)	231.314417 (37.082955)	4.460	0.005*	0.106
Presubiculum body BIL	139.005924 (24.434484)	147.379001 (23.794153)	5.027	0.003*	0.118
Presubiculum body L	144.626923 (26,007946)	151.628096 (25.379298)	4.759	0.004*	0.112
Presubiculum body R	133.384925 (26.104577)	143.129906 (23,904451)	4.215	0.007*	0.101
GC ML DG Body BIL	125.746465 (14.974986)	127.942834 (17.968491)	15.499	<0.001*	0.145
GC ML DG Body L	124.218915 (16.336498)	127.099504 (19.074068)	5.252	0.002*	0.122
GC ML DG Body R	127.274015 (15.725119)	128.786164 (18.246680)	6.023	0.001	0.138
Subiculum Body BIL	223.560664 (27.00871)	234.067875 (29.433013)	7.525	<0.001*	0.167
Subiculum Body L	226.366639 (28.790600)	237.197002 (32.239558)	6.502	<0.001*	0.147
Subiculum Body R	220.754689 (28.646064)	230.938748 (27.567974)	6.993	<0.001*	0.157
CA3 Body BIL	91.755746 (15.525568)	92.642478 (14.571444)	1.264	0.290	0.032
CA3 Body L	85.172657 (17.634214)	88.811114 (14.513769)	1.036	0.379	0.027
CA3 Body R	98.338835 (16.557806)	96.473843 (18.127733)	1.526	0.212	0.039
CA4 Body BIL	109.438936 (13.050909)	111.391833 (14.527730)	5.549	0.001*	0.128
CA4 Body L	107.251894 (14.549379)	110.220738 (15.149596)	4.760	0.004	0.112
CA4 Body R	111.625978 (13.006786)	112.562928 (15.314990)	5.219	0.002	0.122
TAIL					
Hippocampal_tail_BIL	502.732728 (72.787498)	539.854245 (79.205734)	11.239	<0.001*	0.230
Hippocampal_tail_L	491.113313 (84.292342)	536.150415 (76.013522)	11.171	<0.001*	0.229
Hippocampal_tail_R	514.352142 (69.163347)	543.558074 (88.3465032)	9.090	<0.001*	0.194
FISSURE					

hippocampal_fissure_BIL	128.013474 (27.594804)	127.973851 (24.002825)	12.791	<0.001*	0.253
hippocampal_fissure_L	122.452101 (28.104632)	123.727747 (22.554917)	8.665	<0.001*	0.187
hippocampal_fissure_R	133.574848 (31.067424)	132.219955 (28.935576)	12.746	<0.001*	0.253
GLOBAL					
Whole_hippocampal_head_BIL	1578.700614 (157.534230)	1643.601952 (270.717641)	13.899	<0.001*	0.270
Whole_hippocampal_head_L	1564.486578 (177.183704)	1623.874888 (282.889608)	11.435	<0.001*	0.233
Whole_hippocampal_head_R	1592.914651 (156.526390)	1663.329016 (267.759158)	14.048	<0.001*	0.272
Whole_hippocampal_body_BIL	1102.424574 (105.470282)	1140.991984 (146.730328)	12.095	<0.001*	0.243
Whole_hippocampal_body_L	1084.204808 (113.540976)	1127.365636 (143.698447)	9.918	<0.001*	0.208
Whole_hippocampal_body_R	1120.644339 (106.823088)	1154.618332 (153.506826)	12.652	<0.001*	0.251
Whole_hippocampus_BIL	3183.857916 (300.920736)	3324.448181 (472.425237)	15.691	<0.001*	0.294
Whole_hippocampus_L	3139.804700 (327.556841)	3287.390939 (471.957998)	13.858	<0.001*	0.269
Whole_hippocampus_R	3227.911131 (298.470746)	3361.505423 (484.223385)	15.457	<0.001*	0.291

* p values surviving $p < .05$-FDR correction.

Supplementary Table S2: Sociodemographic, and clinical differences between PCS patients with and without blood biomarker assessment

	PCS with biomarkers (n=57)	PCS without biomarkers (n=27)	U / Fisher/ χ^2	*p*
Age	49.60 (11.33)	53.63 (10.77)	641.00	0.218
Sex (women%)	38 (66.67%)	20 (74.07%)	-	0.616
Education (years)	14.79 (3.61)	12.96 (4.05)	579.00	0.055
Days of Evolution	324.36 (123.73)	362.67 (144.72)	674.50	0.361
Premorbid symptoms				
Hypertension	9 (15.78%)	11 (40.74%)	-	0.026
Diabetes	6 (10.52%)	3 (11.11%)	-	1.000
Dyslipidemia	13 (22.80%)	9 (33.33%)	-	0.426
Neurological Symptoms during the acute phase				
Headache	44 (77.19%)	23 (85.18%)	-	0.368
Hyposmia+ageusia	31 (54.38%)	15 (55.55%)	1.100	0.894
Clinical symptoms				
MFIS	53.71 (14.26)	52.33 (16.60)	747.50	0.934
BDI-II	14.09 (8.67)	15.00 (9.91)	722.00	0.741
PSQI	8.72 (4.53)	11.64 (4.52)	450.00	0.008
BSIT	9.28 (2.43)	8.96 (2.18)	638.00	0.305

Values are shown as mean (SD) or n (%).

MFIS = Modified Fatigue Impact Scale; BDI-II = Beck Depression Inventory (II); PSQI = Pittsburgh Sleep Quality Index; BSIT = Brief Smell Identification Test;

Supplementary Table S3: Sociodemographic and clinical details of the seven post-mortem COVID-19 samples

	Age	Sex	Clinical Description
Patients			
1	22	Female	**Background:** Hospital admission for non-infectious pathology SAH due to cerebral aneurysm. **Diagnosis:** Intrahospital infection: 32 days after admission PCR SARS-COV-2 positive. After 48 hours of evolution cardiorespiratory arrest and death.
2	62	Male	**Background:** Hospital admission for non-infectious pathology: appendectomy. After admission PCR SARS COV-2 positive with subsequent evolution of the infection 30 days before death. **Diagnosis:** SARS-CoV-2 pneumonia. Acute respiratory failure with the need for prolonged mechanical ventilation. Enterococcus faecalis bacteremia. Acinetobacter baumanii bacteremia. Neurological data of psychomotor agitation/delirium of a possible toxic-drug cause. Hyperkinetic syndrome of probable toxic-drug cause Acquired weakness of the critically ill. Septic shock and acute anemia.
3	64	Male	**Background:** Hospital admission for non-infectious pathology: appendectomy. After admission PCR SARS COV-2 positive with subsequent evolution of the infection 30 days before death. **Diagnosis:** SARS-CoV-2 pneumonia. Acute respiratory failure with the need for prolonged mechanical ventilation. Enterococcus faecalis bacteremia. Acinetobacter baumanii bacteremia. Neurological data of psychomotor agitation/delirium of a possible toxic-drug cause. Hyperkinetic syndrome of probable toxic-drug cause Acquired weakness of the critically ill. Septic shock and acute anemia.
4	20	Female	**Background:** obesity, kyphoscoliosis, amenorrhea of one year of evolution under study by gynecology, mild mental retardation and conduct disorder. Anxiety depressive syndrome. COVID diagnosis 4 days after gastrointestinal symptoms (epigastralgia) with negative PCR two days prior to diagnosis. 4 days after the death from COVID-19. **Clinical judgment:** Massive pulmonary thromboembolism in a COVID-positive patient. obstructive shock. Fibrinolysis. Cerebral edema. Central transtentorial herniation. Pulmonary embolism and infarction. Cerebral edema.
5	33	Female	**Background:** Dental manipulation (endodontics). 9 days later tonic-clonic crisis in the context of fever and headache and molar pain. Antibiotic treatment and clinical diagnosis of COVID. **Clinical judgement:** CT scan with suspected cerebritis. After death, in anatomy pathology positive staining for SARS-CoV-2.
6	62	Male	**Background:** AHT Hypothyroidism, COVID positive after 7 days of symptoms of fatigue, fever, cough with expectoration and onychophagia. 24 days after death in the ICU. **Clinical judgments:** bilateral pneumonia due to SARS-COV-2 AHT hypothyroidism hypoxemic respiratory failure.
7	73	Male	**Background:** AHT, hyperuricemia, glaucoma, morbid obesity, Hepatic cirrhosis. Well-differentiated colon adenocarcinoma of 0.5 cm, infiltrating, on an adenovillous polyp. Admitted for: To rule out surgical wound infection. **Diagnosis:** Decompensated liver cirrhosis: Hydropic decompensation, Hyponatremia, Acute renal failure, Probable grade I hepatic

			encephalopathy. 8 days after admission PCR SARS-COV-2 positive. 8 days after, death from COVID positive.

Supplementary Table S4: Sociodemographic, and clinical differences between hospitalized and non-hospitalized PCS patients

	PCS Hospitalized (n=28)	PCS Non-hospitalized (n=56)	U / Fisher/ χ^2	*p*
Age	56.64 (11.46)	48.02 (10.06)	429.00	0.001
Sex (women%)	16 (57.14%)	42 (75%)	-	0.133
Education (years)	13.46 (4.66)	14.57 (3.33)	692.00	0.359
Premorbid symptoms				
Hypertension	11 (39.28%)	9 (16.07%)	-	0.029
Diabetes	5 (17.85%)	4 (7.14%)	-	0.152
Dyslipidemia	12 (41.37%)	10 (17.85%)	-	0.019
Neurological Symptoms during the acute phase				
Headache	20 (71.42%)	47 (83.92%)	-	0.148
Hyposmia+ageusia	13 (46.42%)	33 (58.92%)	5.122	0.275
Clinical symptoms				
MFIS	53.89 (15.22)	52.95 (14.98)	738.00	0.758
BDI-II	14.32 (9.12)	14.42 (9.09)	769.00	0.992
PSQI	9.36 (5.63)	9.74 (4.19)	695.00	0.549
BSIT	9.04 (2.76)	9.25 (2.12)	758.50	0.911

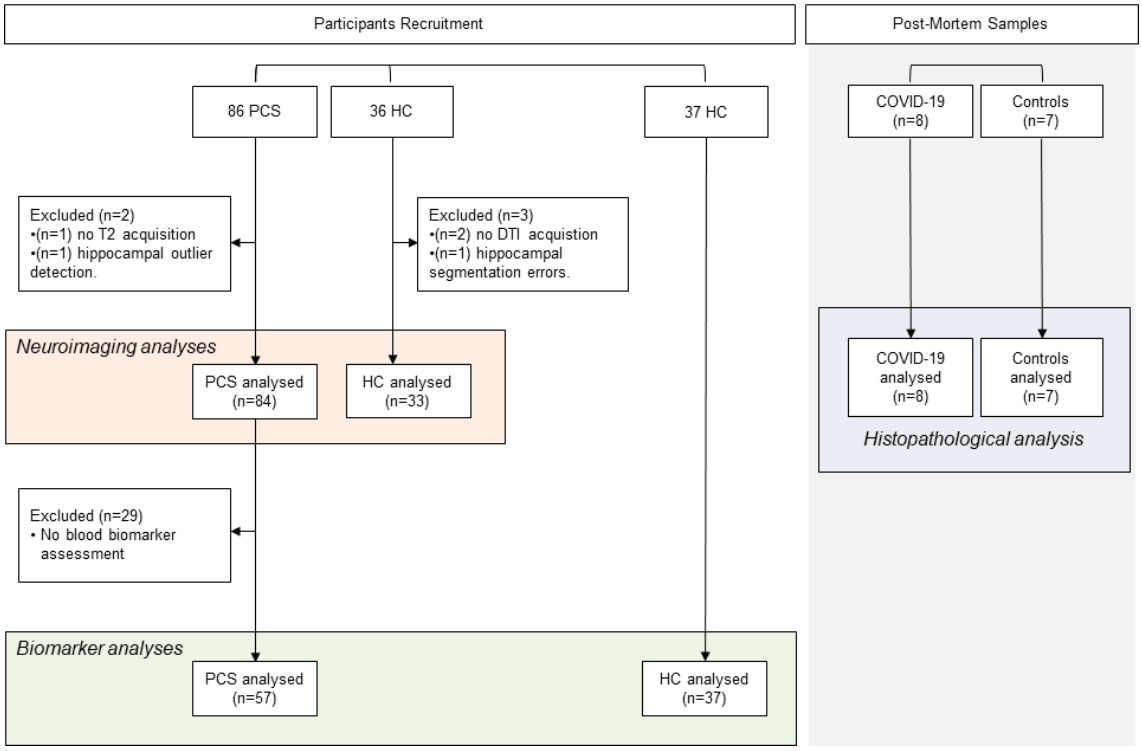
Values are shown as mean (SD) or n (%).

MFIS = Modified Fatigue Impact Scale; BDI-II = Beck Depression Inventory (II); PSQI = Pittsburgh Sleep Quality Index; BSIT = Brief Smell Identification Test;

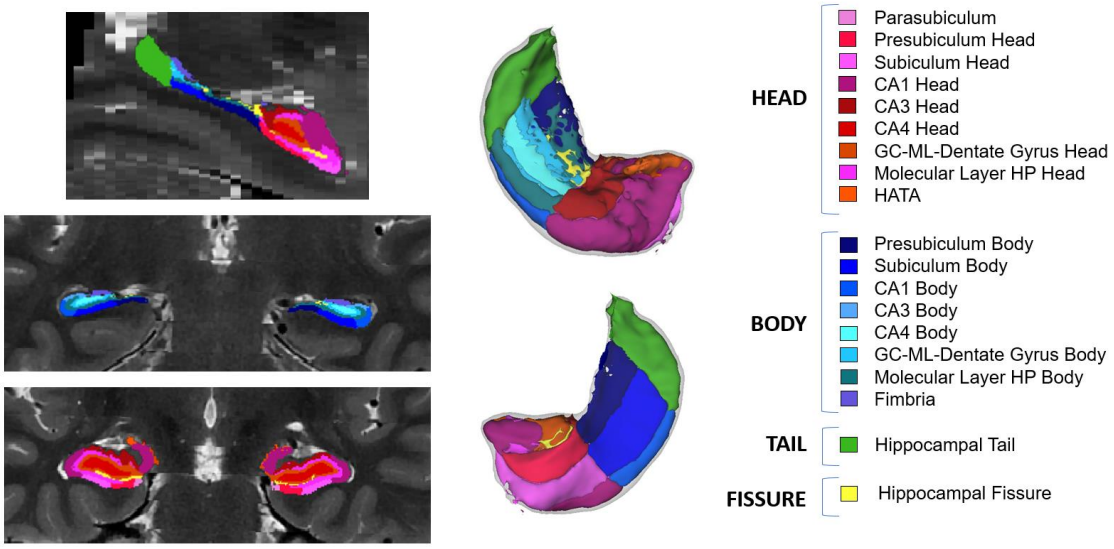
Supplementary Table S5: Neuropsychological results in PCS

		Raw Score	Max – Min score	Impairment (%)*	
				≤ 5 (1.65 SD)	≤ 7 (1 SD)
Neuropsychological results					
Digit Span	Forward	5.90 (1.54)	2-9	9.5%	20.2%
	Backward	4,07 (1,23)	2-7	9.5%	22.6%
Corsi test	Forward	5,37 (1,19)	2-8	9.5%	10.7%
	Backward	4,63 (1,15)	2-7	7.1%	22.6%
SDMT		42,90 (12,91)	8-67	10.7%	28.6%
FCSRT	Free Recall Trial 1	7,61 (2,34)	2-15	1.2%	11.9%
	Total Free Recall	27,85 (7,47)	8-43	15.5%	31.0%
	Total Recall	40,06 (8,10)	4-48	25%	40.5%
	Delayed Free Recall	10,19 (3,62)	0-16	16.7%	28.6%
	Delayed Total Recall	14,04 (2,65)	4-16	16.7%	31%
ROCF	Copy (score)	32,46 (3,84)	19-36	3.6%	14.3%
	Copy (Time)	138,11 (65.35)	41-414	-	9.5%
	Recall (3 mins)	18,35 (6,33)	4.5-34	3.6%	11.9%
	Recall (30 mins)	18,23 (6,78)	4.5-39	3.6%	14.3%
	Recognition	19,05 (2,38)	12-23	13.1%	31%
Verbal Fluency	Phonetic P	15,50 (5,54)	4-32	9.5%	23.8%
	Phonetic M	13,17 (4,27)	2-25	6.2%	12.3%
	Phonetic R	12,63 (4,13)	2-23	2.5%	10%
	Semantic	20,69 (5,23)	11-32	9.5%	27.4%
Stroop	Words	91,19 (22,14)	40-131	23.8%	42.9%
	Color	62,01 (15,55)	24-102	28.6%	39.3%
	W-C	36,85 (11,76)	12-82	19%	38.1%
BNT		51,68 (5,77)	34-60	6.0%	19%
JLO		20,55 (6,57)	0-30	19%	34.5%
VOSP	Object Decision	16,57 (2,41)	8-20	3.6%	23.8%
	Pr. Silhouettes	9,35 (3,18)	4-20	8.3%	23.8%
	Position Discrimination	18,50 (3,06)	2-20	13.1%	31%
	Number Localization	9,31 (2,44)	4-20	13.1%	31%

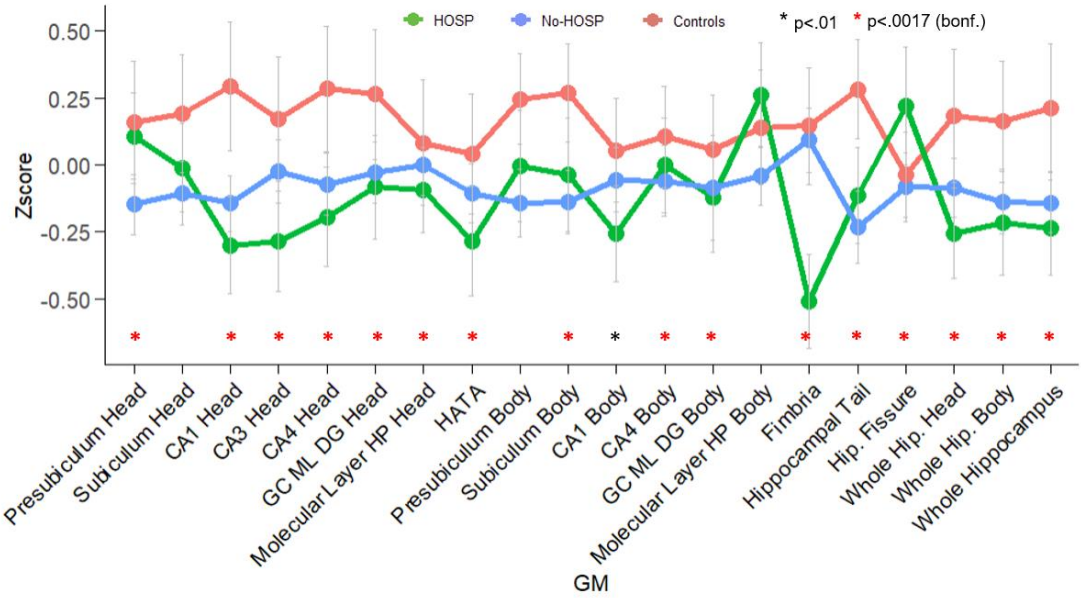
*Impairment = Percentage of patients showing ≤ 5 or ≤ 7 in the scaled score in cognitive tests. SD = Standard Deviation. Stroop W= Stroop Words; Stroop C = Stroop Color; Stroop WC= Stroop Word-Color; SDMT= Simbol Digit Modality Test; ROCF= Rey-Osterrieth Complex Figure; VOSP= Visual Object and Space Perception Battery; JLO= Benton Judgment Line Orientation; BNT= Boston Naming Test.



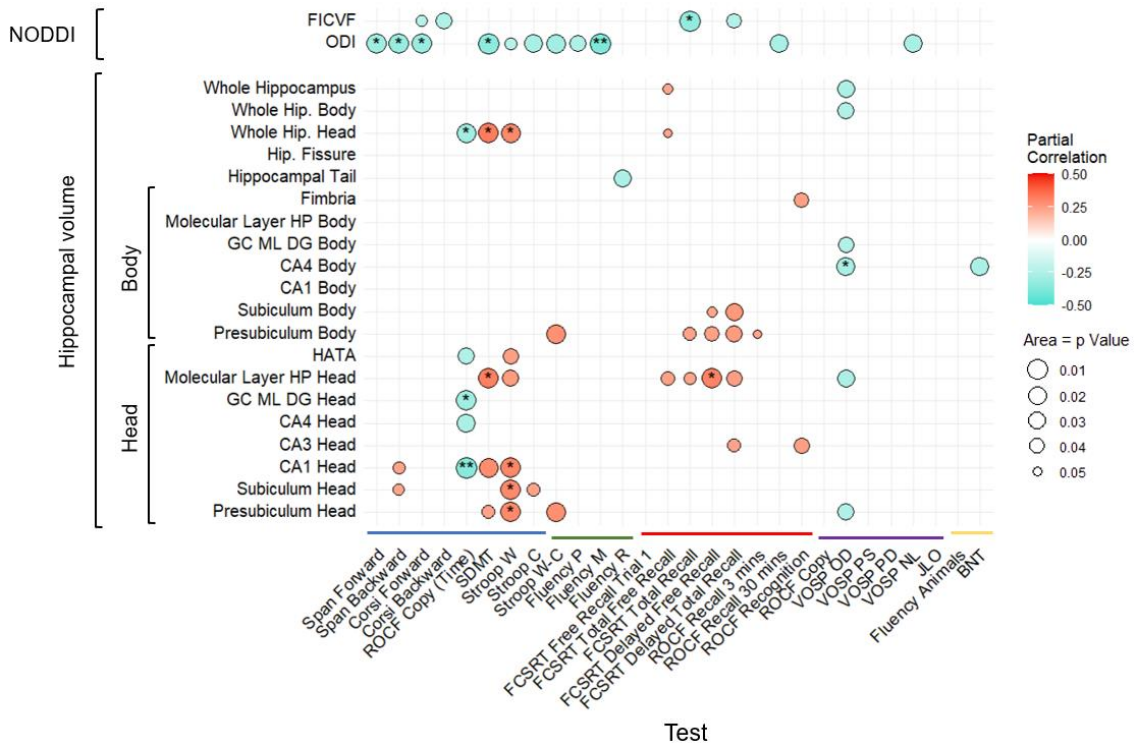
Supplementary Fig. S1: Recruitment flow-chart.



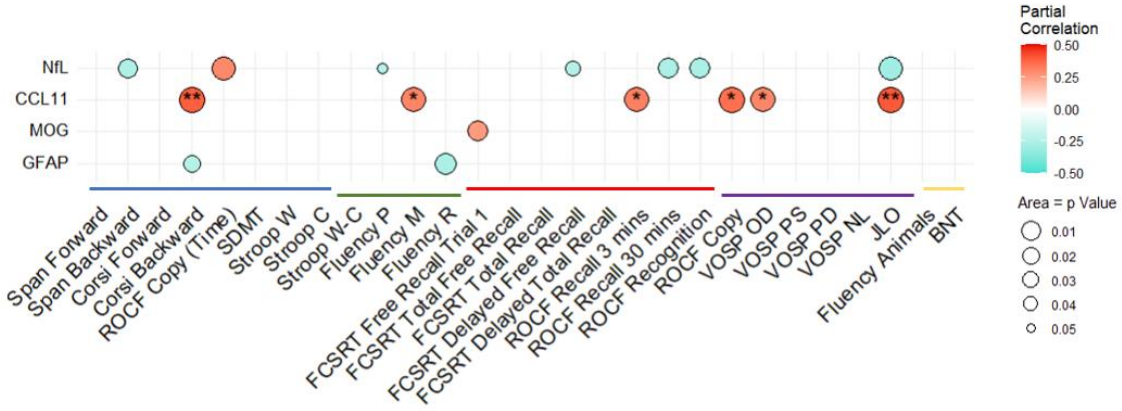
Supplementary Fig. S2: Hippocampal subfield segmentation in Freesurfer.



Supplementary Fig. S3: Hippocampal subfield volume differences in hospitalized patients compared to non-hospitalized patients. Mean (z-scores) and standard error of hippocampal subfield volume differences in hospitalized patients compared to non-hospitalized patients. HC group is included for reference only.



Supplementary Fig. S4: Associations between hippocampal subfield volume and cognition in PCS. Significant correlations between microstructural and hippocampus subfields volume (bilateral) with cognition ($p < 0.05$). *$p<0.01$ and **$p<0.0017$ (Bonferroni corrected). Blue = Attention, processing speed and working memory; Green = Executive Functions; Red = Learning and Memory; Purple = Visuoperceptive, visuospatial and visuoconstructive ability; Yellow = Language. ROCF = Rey-Osterrieth Complex Figure; SDMT = Symbol Digit Modalities Test; Stroop W= Stroop Word subtest; Stroop C = Stroop Color subtest; Stroop W-C = Stroop Word-Color Interference subtest; FCSRT = Free and Cued Selective Reminding Test; VOSP = Visual Object and Space Perception Battery; JLO = Judgment Line Orientation; BNT = Boston Naming Test.



Supplementary Fig. S5: Associations between blood biomarkers and cognition in PCS. Significant correlations between blood biomarkers with cognition ($p < 0.05$). *$p<0.01$ and **$p<0.0017$ (Bonferroni corrected). Blue = Attention, processing speed and working memory; Green = Executive Functions; Red = Learning and Memory; Purple = Visuoperceptive, visuospatial and visuoconstructive ability; Yellow = Language. ROCF = Rey-Osterrieth Complex Figure; SDMT = Symbol Digit Modalities Test; Stroop W= Stroop Word subtest; Stroop C = Stroop Color subtest; Stroop W-C = Stroop Word-Color Interference subtest; FCSRT = Free and Cued Selective Reminding Test; VOSP = Visual Object and Space Perception Battery; JLO = Judgment Line Orientation; BNT = Boston Naming Test.