SUPPLEMENTARY MATERIAL

Supplementary Methods

1. Neuropsychological test battery

In a subgroup of patients (n = 13) cognitive functions were examined with a 45-min cognitive battery consisting of six standardized neuropsychological tests. The test battery was administered by a trained neuropsychologist in an undisturbed environment in German (native) language. The neuropsychological test battery comprised the Hopkins Verbal Learning Test revised (HVLTR)[1], Digit Span forward/reverse[2], Trail Making Test part A and B[3], Color-Word Interference Test (FWIT)[4], the Symbol-Digit Modalities Test (SDMT)[5], and a semantic and letter fluency test[6]. For each test, z-scores were calculated based on the respective mean and standard deviation, stratified by age and education[7]. For the Color-Word Interference Test (FWIT)[4], which did not provide mean and standard deviation, percentile ranks or T-scores were transformed into z-scores. Results of n = 11 patients were previously reported[8].

Supplementary Results

1. Results of the Neuropsychological test battery

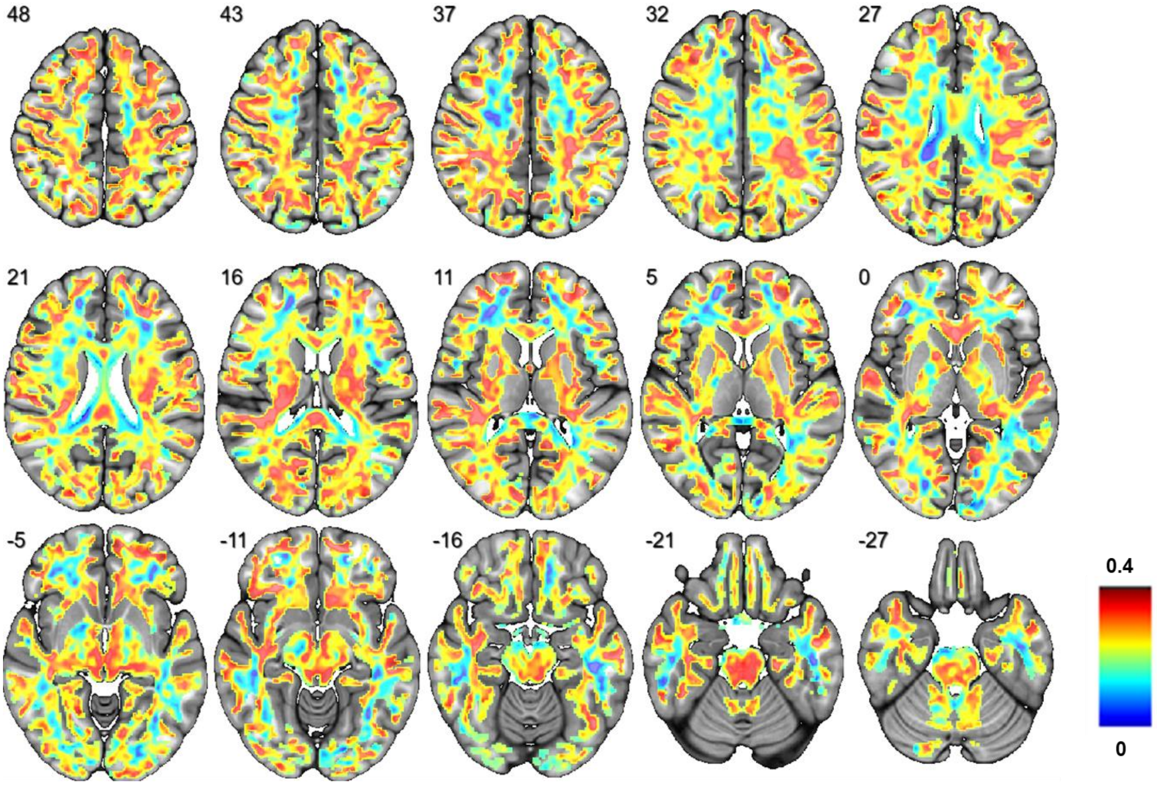
Detailed results are displayed in the **Supplementary Table 1**. The Digit Span backward was affected most frequently (6/13), followed by semantic fluency (5/12; both representing executive functions). Moreover, deficits were present in the Hopkins Verbal Learning Test revised (HVLTR; 5/12), representing the cognitive domain memory. Tests for attention were less frequently impaired. Overall, these findings confirmed the results from the MoCA.

2. Confirmatory analysis with AMICO-NODDI

To corroborate the results of our Bayesian model, we also extracted diffusivity parameters using the accelerated microstructure imaging via convex optimization (AMICO)-NODDI, a regularized version of NODDI that also allows fast processing times due to the linearization of fitting procedures (https://github.com/daducci/AMICO)[9]. From the parameters provided by the AMICO approach, V_{iso} can be considered as the homologue of V-CSF. In a comparison of whole-brain white matter V_{iso} parameters between COVID-19 patients and controls

(ANCOVAs controlling for "age" and "sex"), a highly significant increase ($P < 0.001$; df: 51, $t = -4.4$; Cohen`s d: -1.0) was present in COVID-19 similar to our V-CSF data. The distribution of standardized regression coefficients attained by voxel-wise comparisons (COVID-19 vs. controls, nuisance covariates "age", "sex" and "tissue probability value") also confirmed a widespread increase of V_{iso} (see **Supplementary Figure 1**) – although the frontoparietal maxima are a bit less clearly pronounced compared to V-CSF data. Using partial Pearson's correlation approach controlling for sex and age, significant correlations could be detected between V_{iso} and MoCA-performance ($r = -0.3$; $P = 0.042$) as well as V_{iso} and the PES ($r = 0.59$; $P = 0.042$). For olfactory performance, no significant correlation was present ($r = 0.16$; $P = 0.6$). For interleukin-6, a statistically non-significant trend towards a correlation to V-CSF emerged ($r = 0.47$; $P = 0.078$).

Supplementary Figures



Supplementary Figure 1. The standardized regression coefficients of the factor V_{iso} were extracted from regression models attained by voxel-wise comparisons between COVID-19 patients and controls (with covariates "age", "sex" and "tissue probability value") and were superimposed onto a T1w MRI template. Color-coding indicates the coefficient values as a measure of effect size of the factor "COVID-19" on V_{iso} (hot colors: large effect size vs. cold colors: small effect size). Please note that all coefficients monodirectionally indicated an increase in V_{iso}. Radiological orientation, i.e. left image side corresponds to patient's right body side; numbers denote the axial (z) position in millimetres.

Supplementary Tables

Supplementary Table 1: Baseline characteristics of COVID-19-patients (n=20)	
Baseline Characteristics	**n (%) or mean (SD); range**
Body Mass Index (BMI)	27.8 (4.5); 19.6 to 35.9
Weight (kg)	81.7 (15.1); 53.7 to 112
Height (cm)	171.6 (9.2); 150 to 183
Systolic BP (mmHg) at discharge	131.2 (10.5); 115 to 150
Diastolic BP (mmHg) at discharge	75.3 (12.7); 55 to 105
Smoker status (current)	2 (10%)
Alcohol consumption (> 3days/week)	3 (15%)

Supplementary Table 2: Characteristics of healthy controls (n=35)	
Demographic data	**n (%) or mean (SD); range**
Age (years)	51.8 (17.3); 21 to 81
Sex (male / female)	18 (51) / 17 (49)
Baseline Characteristics	**n (%) or mean (SD); range**
Body Mass Index (BMI)	24.8 (2.6); 20.8 to 30.6
Smoker status (current)	1 (3%)
Alcohol consumption (> 3days/week)	0 (0%)
Comorbidities	**n (%)**
Bronchial asthma	2 (6%)
Coronary heart disease	1 (3%)
Deep vein thrombosis	1 (3%)
Malignancies	4 (12%)
Clinical readouts	**mean (SD); range**
MoCA sum score (corrected for years of education)	28.3 (1.5); 26 to 30

Supplementary Table 3: Detailed results of the neurocognitive test battery (n = 13); n = 11 are a subsample of previously published patients[8]

Test	Domain	Outcome Variable	Mean Z-Score ± SD	N (%) ≤ -1,5 SD
Hopkins Verbal Learning Test revised (HVLTR): learning (n = 12)	Verbal Memory	Scores	-1.01 ± 1.39 [-3.22 – 1.10]	5 (42 %)
HVLTR: delayed recall (n = 12)	Verbal Memory	Scores	-0.58 ± 0.94 [-2.01 – 0.58]	3 (25 %)
HVLTR: recognition discrimination index (n = 12)	Verbal Memory	Scores	-0.17 ± 1.11 [-2.49 – 0.81]	2 (17 %)
Color-Word Interference reading (n = 12)	Processing Speed	Time (s)	-0.57 ± 1.24 [-2.60 – 1.60]	4 (33 %)
Color-Word Interference: naming (n = 12)	Processing Speed	Time (s)	-0.32 ± 1.16 [-1.90 – 1.70]	2 (17 %)
Symbol-Digits-Modalities Test (n = 12)	Processing Speed	Time (s)	-0.76 ± 1.14 [-2.54 – 0.90]	3 (25 %)
Trail Making Test A (n = 13)	Attention	Time (s)	-0.05 ± 0.93 [-1.57 – 1.30]	1 (8 %)
Digit Span forward (n = 13)	Attention	Score	0.07 ± 1.19 [-1.81 – 2.51]	2 (15 %)
Digit Span backward (n = 13)	Executive function	Score	-1.29 ± 1.19 [-1.81 – 2.15]	6 (46 %)
Semantic fluency (n = 12)	Executive function	Score	-0.85 ± 1.27 [-2.79 – 1.05]	5 (42 %)
Phonemic fluency (n = 12)	Executive function	Score	-0.22 ± 1.14 [-1.87 – 1.50]	2 (17 %)
Color-Word Interference: interference (n = 12)	Executive function	Time (s)	-0.21 ± 1.07 [-2.40 – 1.20]	2 (17 %)
Trail Making Test B (n = 13)	Executive function	Time (s)	-0.29 ± 1.06 [-1.81 – 1.45]	2 (15 %)

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