CSF and Blood Analyses in Participants with Post-COVID-19 Neuropsychiatric Symptoms

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This study of post-COVID participants with neuropsychiatric symptoms and mostly mild COVID illnesses revealed elevated levels of serum **GFAP** (a reactive astrocyte marker), serum **D-dimer**, serum and CSF **anti-SARS-CoV-2 antibodies**, and CSF **monocytes** when compared to pre-pandemic controls. Notably there were **no differences** in biomarkers of microglial activation, neuronal injury, and CNS inflammation.

Background

- The pathogenesis of neuropsychiatric symptoms persisting months after acute SARS-CoV-2 infection is poorly understood.
- We examined clinical and laboratory parameters in participants with post-acute COVID-19 neuropsychiatric symptoms in order to assess for systemic and nervous system immune alterations.

Methods

- Participants with a history of laboratory confirmed COVID-19 and ongoing neurologic symptoms were enrolled in an observational study.
- We collected medical history and paired cerebrospinal fluid (CSF) and blood.
- Neopterin, NfL, tau, GFAP, YKL-40, sTREM2, and anti-SARS-CoV-2 anti-spike, RBD, and nucleocapsid antibodies were measured by standard ELISA in CSF or ultrasensitive Simoa platform immunoassay in serum.
- Non-parametric tests were used.

Figure 1. Blood

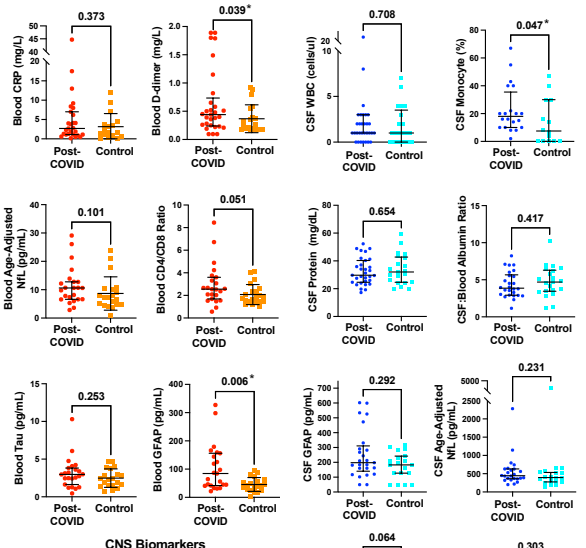


Figure 2. CSF

Table 1. Demographics

	Post-COVID (n = 34)	Controls (n = 21)	Comparison
	Median (IQR); Percent (Count)		P-value
Age	53 (40 - 62)	48 (40 - 55)	0.1404
Female	74% (25)	24% (5)	0.0006
Race/Ethnicity			0.0181
Black	18% (6)	43% (9)	
White	68% (23)	24% (5)	
Hispanic	12% (4)	29% (6)	
Other	3% (1)	5% (1)	
Days from Symptom Onset	300 (132 - 365)		
Level of Care			
Home	74% (25)		
Floor	21% (7)		
ICU	6% (2)		
PASC Symptom			
Cognitive Impairment	76% (26)		
Mood symptoms	59% (20)		
Headache	59% (20)		
Neuropathy	35% (12)		
Pre-existing neurologic condition	24% (8)		
Migraine	21% (7)		
Previously on psych med	29% (10)		

Figure 3. Antibodies

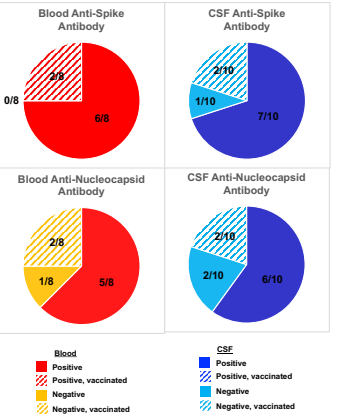


Figure 4. Acute COVID Symptoms

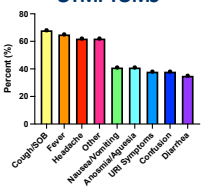
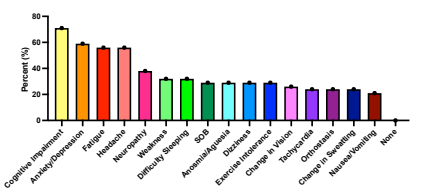


Figure 5. Post-COVID Symptoms



Results

- The demographics for the post-COVID participants (n=34) and controls (n=21) cohorts are detailed in **Table 1**.
- In blood (**Figure 1**), D-dimer (median 0.44 vs 0.26 mg/L; p = 0.039) and GFAP (median 84.4 vs 42.4 pg/mL; p=0.0064) were higher in post-COVID.
- In **Figure 2**, the frequency of CSF monocytes was higher (18% vs 7.5%; p=0.047), and there was a trend toward sTREM2 elevation (1653 vs 1317pg/mL; p=0.064) in the post-COVID cohort.
- Antibodies against at least one SARS-CoV-2 antigen were detected in 7/10 CSF and 8/8 blood samples in the post-COVID group (**Figure 3**).

Conclusions

- Deeper immunophenotyping in a larger cohort may provide greater insight into neuropathogenesis.

No Disclosures
Funding: R21MH118109; R01MH125737; K23MH118999; R01AI157488-01; Merck Investigator Studies Program
Acknowledgements: Thank you to all participants

UCSF University of California San Francisco
University of Gothenburg
Yale School of Medicine