Focal Cerebral Hypoperfusion in Individuals With Cognitive Impairment After COVID-19

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Background

- A routine clinic MRI of the brain has little value in diagnosing or treating long COVID. The most common findings are non-specific, including white matter lesions, enlarged perivascular spaces, and microbleeds.[1]
- Gray matter volume alterations in limbic, orbitofrontal, and secondary olfactory cortices are present in long-COVID patients and may change over time.[2]
- Preliminary evidence of hypoperfusion in the frontal, parietal, and temporal cortices.[3]
- Cognitive impairment is a common neuropsychiatric post-COVID-19 condition and is often associated with fatigue, post-exertional malaise, and dysautonomia.
- We investigated for vascular hypoperfusion in individuals with self-reported cognitive impairment compared to post-COVID-19 controls without a PCC.

Methods

- Participants with N-PCC (new self-reported cognitive impairment >3 months after COVID-19) and post-COVID-19 controls with no PCC underwent a cross-sectional clinical assessment (surveys, chart review) and blood collection.
- **Procedures**: MRI of the brain with Arterial Spin Labeling (ASL) to measure cerebral blood flow (CBF) in ml/100g/min.
  - Non-parametric multiple Mann-Whitney testing of CBF between groups by region using the Harvard-Oxford atlas (48 regions).
  - T-tests of CBF between groups on a voxel level ($1\times1\times1mm^3$) using BioImage Suite.
- **Exclusion Criteria**: <18 years old, pregnant, drug use, history of dementia, stroke, or other major neurologic/psychiatric illness.

Results

- The two groups were similar demographically and in terms of vascular risk factors, except for a higher prevalence of hyperlipidemia in the N-PCC group (**Table 1**).
- The prevalence of PCC symptoms is detailed in **Figure 2**.
- In the voxel-based analysis, there was a difference in CBF between the two groups in the left greater than right parietal lobes (Figure 2A).
- In the region-based analysis, CBF was reduced in the right and left superior parietal lobules as well as the post central gyrus and precuneus between the two groups (**Figure 1B**).
- The superior parietal lobule is involved in attention, visuospatial perception, and the representation and manipulation of objects in space.
- The left post-central gyrus is involved in right sided primary somatosensory cortex and proprioception.
- The precuneus overlaps with the superior parietal lobule. It covers a wide range of tasks and networks, including memory, perception of the environment, mental imagery, episodic memory retrieval, and affective responses to pain.
  - The precuneus is affected in early Alzheimer's disease with deposition of amyloid plaques and neurofibrillary tangles.
  - This region of the brain is vulnerable vascular insults given it is supplied by the anastomoses of the anterior, middle, and posterior cerebral arteries.

Preliminary results suggest a trend of hypoperfusion in the left greater than right parietal lobes in individuals with persistent cognitive impairment ("brain fog") over one year after COVID-19 compared to controls

Figure 1. Results Detailed cerebral blood flow (mL/100 g/min) results are presented in A) a voxel-based analysis comparing N-PCC to controls with blue representing significant differences at the $p \leq 0.05$ level and B) a region-based analysis showing the four regions out of 48 where there was a difference between groups.

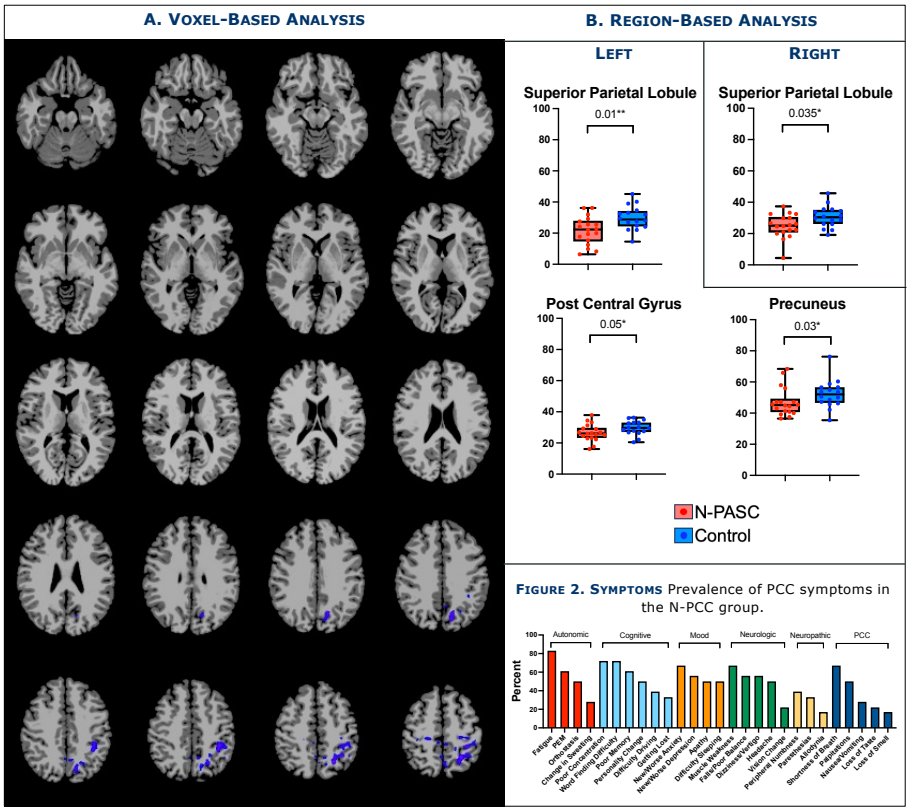


Figure 2. Symptoms Prevalence of PCC symptoms in the N-PCC group.

Table 1. Demographics

	N-PCC N = 18 Median [IQR] | N (%)	Control N = 17 Median [IQR] | N (%)	P-Value
Age (years)	43 [40-57]	40 [32-44]	0.21
Female Gender	14 (78%)	13 (76%)	0.99
BMI (kg/m2)	27 [23-29]	27.5 [24-35]	0.46
Race			0.12
Black	2 (11%)	6 (35%)	
White	16 (89%)	11 (65%)	
Ethnicity			0.99
Hispanic	1 (6%)	1 (6%)	
Hospitalized for Acute COVID-19	6 (33%)	0 (0%)	
Days Since Acute COVID-19	444 [346-720]	619 [502-830]	0.49
Vascular Risk Factors			
Smoking History			0.46
Never	13 (72%)	8 (47%)	
Current	1 (6%)	2 (12%)	
Former	3 (17%)	5 (29%)	
Hypertension	2 (11%)	2 (12%)	0.99
Diabetes	2 (11%)	2 (12%)	0.99
Hyperlipidemia	5 (28%)	0 (0%)	0.045*
Cardiac Disease	0 (0%)	0 (0%)	-
Mental Health			
Anti-Depressant	3 (17%)	5 (29%)	0.44
Medications			
Statin	1 (6%)	1 (6%)	0.99
Anti-Hypertensive	0 (0%)	0 (0%)	-

Conclusions

- There is a trend of hypoperfusion in the left greater than right parietal lobes in individuals with cognitive impairment ("brain fog") after COVID-19 compared to controls without a post-COVID condition.
- Dysfunction in this region may contribute to attention, visuospatial deficits, and episodic and semantic memory impairment.
- We hypothesize persistent microvascular dysfunction is contributing to cognitive impairment after COVID-19.
- In future studies, we hope to identify treatment targets that may improve microvascular function and brain perfusion.

We have no relevant disclosures

Limitations: These are preliminary results from an ongoing study; The sample size is small and there is no pre-pandemic MRI comparison; We did not adjust for multiple comparisons.

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Citations:

[1] PMID: 37568896
[2] PMID: 35255491
[3] PMID: 37037833
[4] PMID: 35320385

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