

# Altered Neurovascular Coupling Underlying Neuropsychiatric Symptoms In Elderly Patients With Long Covid

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## Background

- **High Prevalence:** Neuropsychiatric symptoms such as depression, anxiety, sleep disturbance, fatigue, and post-traumatic stress are highly prevalent in Long COVID.
- **Clinical Parallels:** These symptoms strongly resemble the early behavioral and affective changes observed in aging, vascular cognitive impairment, and Alzheimer's disease.
- **Knowledge Gap:** Despite clinical significance, the neurovascular mechanisms underlying persistent neuropsychiatric symptoms in Long COVID remain poorly understood.

## Objective

- 1) To assess the link between Long COVID neuropsychiatric burden and neurovascular dysfunction.
- 2) To evaluate how these alterations contribute to vascular cognitive impairment.

## Methods

### Participants

- 65 individuals with Long COVID (age:  $60.2 \pm 11.0$ ; 81.5% female) and 73 closely matched controls (age:  $62.9 \pm 8.2$ ; 60.3% female).

### Neuropsychiatric Symptoms

- Neuropsychiatric symptoms were measured using validated scales for insomnia, fatigue, post-traumatic stress, anxiety, and depression.

### MRI acquisition

- 3T MR scan (Signa Premier, GE Healthcare, Waukesha, WI) to assess resting-state functional MRI:
  - Amplitude of Low-Frequency Fluctuations (ALFF) → Arterial spin labeling to quantify cerebral blood flow.
  - Regional homogeneity (ReHo) → Neural synchronization.

### Analyses

- T-tests, ANOVA, and multivariable analyses were conducted to compare the controls and Long COVID groups on ALFF, ReHo, and cognitive metrics.

## Results

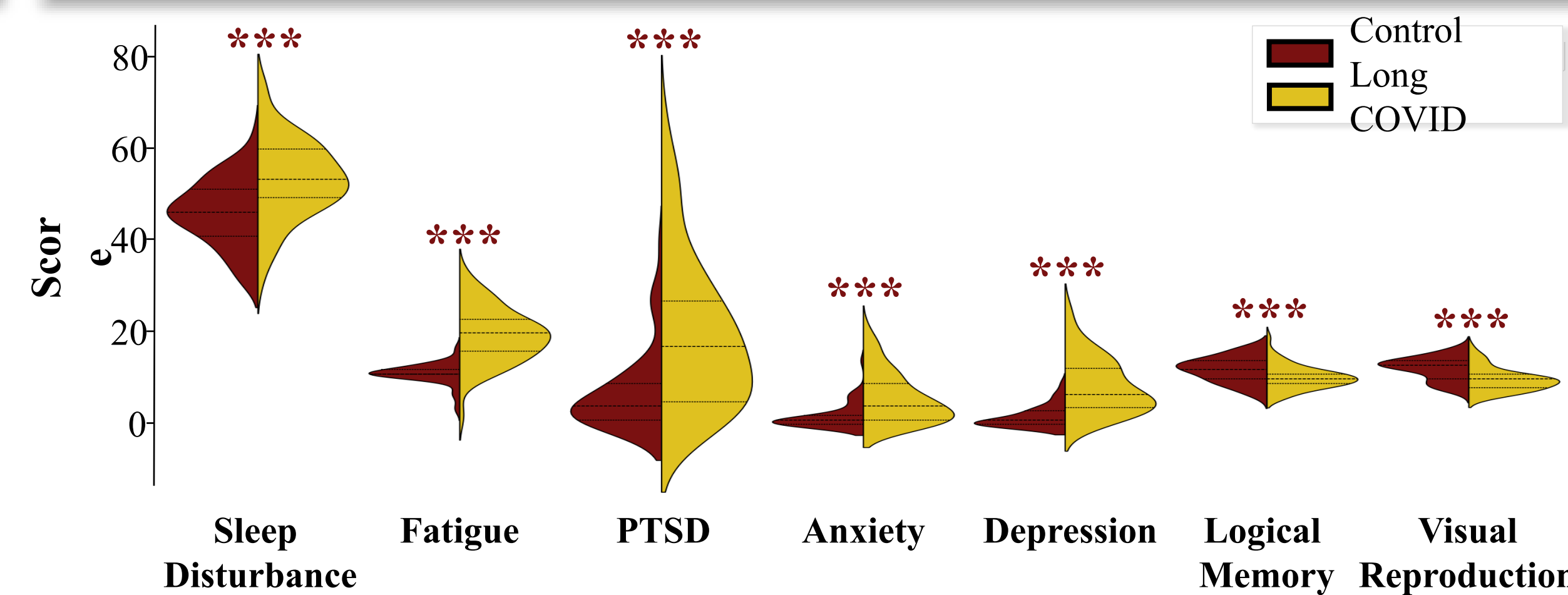


**Figure 1.** Split violin plots demonstrating the distribution of self-reported neuropsychiatric symptoms and cognitive performance in controls vs Long COVID patients. \*\*\* $p < 0.001$ .

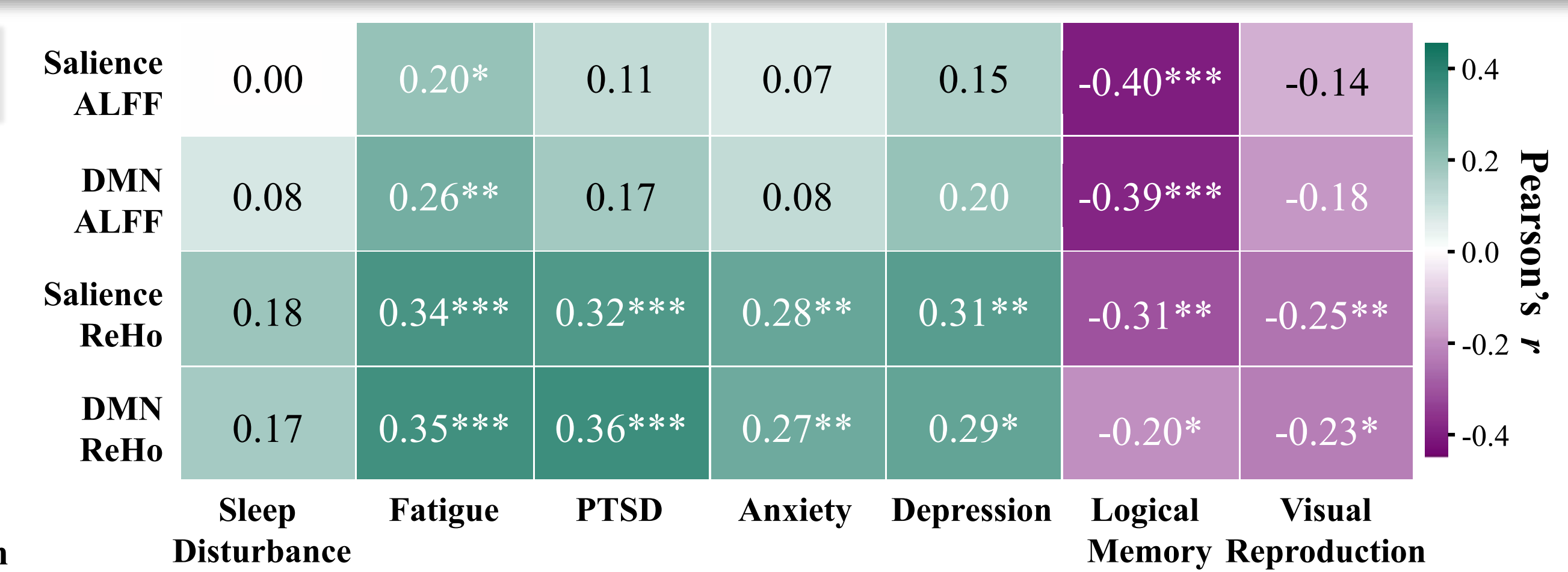


**Figure 2.** Cross-correlation matrix evaluating the direct relationship between regional neurovascular metrics and clinical symptom severity. \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ .

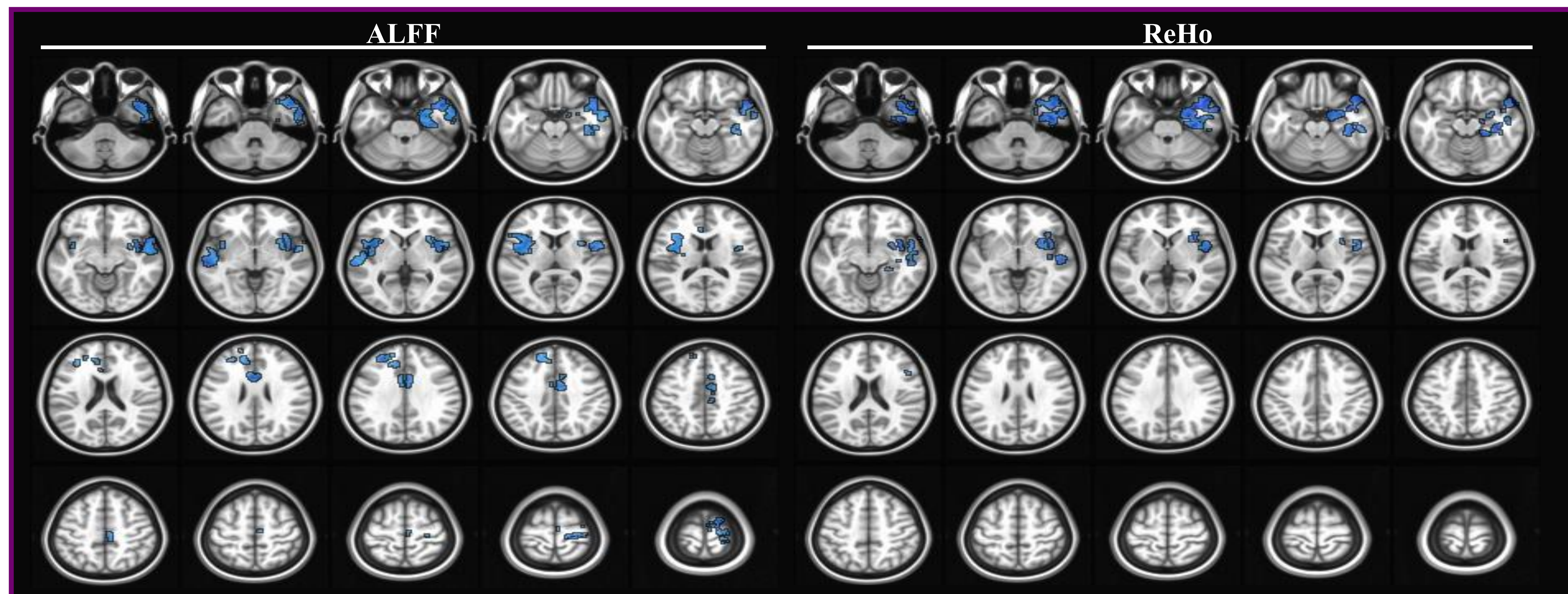


**Figure 3.** Voxel-wise analysis found regions with significantly higher ALFF and ReHo in Long COVID vs controls ( $p < 0.05$ , corrected for multiple comparisons).

## Discussion

- **Network Dysregulation:** Elevated ALFF/ReHo in the Salience and Default Mode Networks were significantly associated with greater psychiatric symptom severity in Long COVID, indicating persistent intrinsic network hyperactivity.
- **Cognitive Impact:** Increased resting-state network activity correlated with poorer memory performance, suggesting that heightened baseline activity may impose a measurable cognitive burden.
- **Mechanistic Implication:** This pattern is consistent with a neurovascular uncoupling framework, in which sustained metabolic demand may not be adequately supported by cerebral perfusion.
- **Clinical Relevance:** Neurovascular uncoupling may serve as a quantifiable marker of disease burden and a potential therapeutic target to mitigate longer-term cognitive sequelae, pending longitudinal confirmation.

## References

1. Boutet M, Salmam I, Roy JS, et al. *Disabil Rehabil*. 2025;47(26):6881-6888. doi:10.1080/09638288.2025.2521000
2. Ajčević M, Iskra K, Furlanis G, et al. *Sci Rep*. 2023;13(1):5808. doi:10.1038/s41598-023-32275-3

## Acknowledgements

This work is partially supported by the Daniel M. Soref Charitable Trust and the organizations below. Thank you!