

A Frontal Hypermetabolism Pattern in Long COVID Identified by FDG-PET across Two Independent Pipelines

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Two independent analytical FDG-PET pipelines identified a convergent, frontal-predominant hypermetabolic pattern extending to cingulate and left parietal regions in patients with long COVID more than two years after infection.

BACKGROUND

ANALYSIS PIPELINE

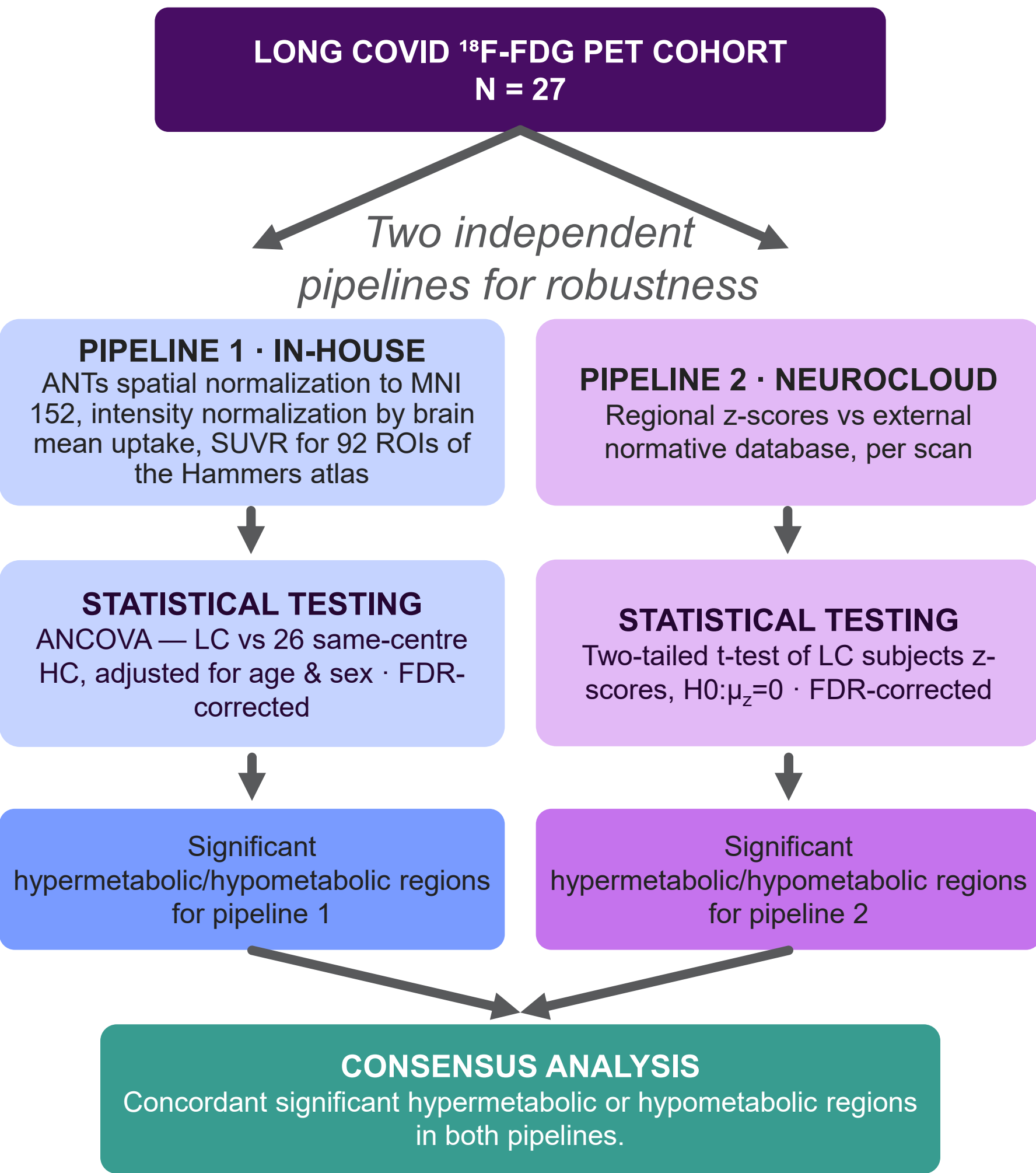
RESULTS

CONCLUSIONS

Long COVID (LC) is marked by cognitive symptoms persisting at least three months after SARS-CoV-2 infection [1,2]. FDG-PET findings in LC are heterogeneous and hard to interpret, owing to varied healthy-control groups, different intensity-normalisation strategies, and assessment soon after infection [3]. Here we study brain metabolism in patients with cognitive symptoms persisting more than two years after infection, using two independent pipelines with distinct controls and normalisation strategies.

STUDY DESIGN

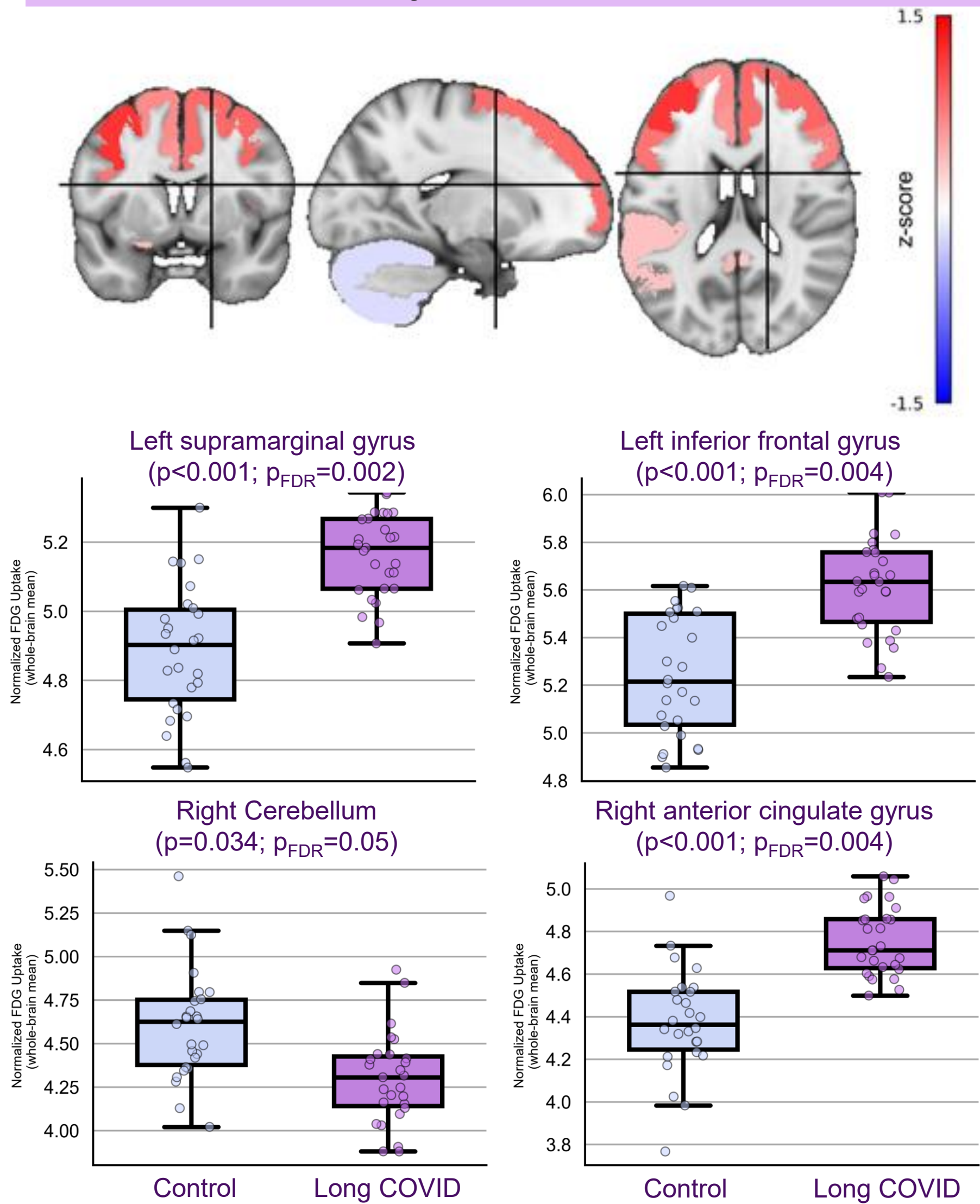
- **Design:** cross-sectional study, Buenos Aires, Argentina
- **Inclusion:** cognitive complaints >3 mo after confirmed SARS-CoV-2; age 30–65; no prior neuro / psychiatric disease
- **Cohort:** 168 LC recruited → 27 with brain [¹⁸F]FDG-PET
- **Assessment:** neurological exam, questionnaires, neurocognitive battery, MRI for the 168 LC
- **PET scan:** Philips Vereos TOF PET-CT
- **Analysis:** two independent PET pipelines; consensus = concordant regions only



	Long COVID full cohort (N = 168)	Long COVID 18F-FDG PET subcohort (N = 27)	Healthy Brain FDG-PET (N = 26)
Age, years (mean ± SD)	48.7 ± 8.3	47.4 ± 9.8	63.4 ± 15.5
Female, n (%)	123 (73.2%)	17 (63%)	16 (61.5%)
Days since first infection, mean ± SD)	686.6 ± 334.3	697.5 ± 334.7	-

Consensus analysis identified hypermetabolism in 15 frontal, parietal and cingulate regions, together with focal hypometabolism in the right cerebellum. All reported regions showed concordant alterations across the in-house and Neurocloud pipelines.

Consensus metabolic pattern across both pipelines. Only directionally concordant significant regions are displayed. Colours indicate mean Neurocloud regional z-scores.

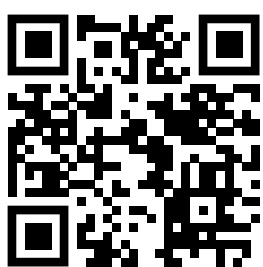


Two complementary FDG-PET pipelines identified a frontal-predominant hypermetabolic pattern extending to bilateral cingulate and left inferior parietal regions more than two years after infection. This persistent pattern may reflect compensatory neural recruitment or chronic neuroimmune activation, although FDG-PET cannot distinguish between these mechanisms. Cross-pipeline agreement supports the robustness of the findings, but interpretation is limited by the modest sample and age imbalance despite statistical adjustment.

REFERENCES

- [1] Nalbandian A et al. Post-acute COVID-19 syndrome. Nat Med 2021 274. 2021 Mar 22;27(4):601–15.
- [2] Andrade BS et al. Long-COVID and Post-COVID Health Complications: An Up-to-Date Review on Clinical Conditions and Their Possible Molecular Mechanisms. Viruses. 2021 Apr 1;13(4):700.
- [3] Meyer P, Hellwig S, Blazhenets G, Hosp J. Molecular Imaging Findings on Acute and Long-Term Effects of COVID-19 on the Brain: A Systematic Review. J Nucl Med. 2022 Feb 17;63:971–80.

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