

A Multicentre FDG-PET and Cytokine Study

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KEY POINTS

01. We identified frontal & parietal hypermetabolism across two independent FDG-PET pipelines.

03. Reduced anti-inflammatory IL-10 alongside elevated pro-inflammatory markers (MCP-1 and IL-17A) supports a shift toward a pro-inflammatory state.

02. We found ↑ MCP-1 & IL-17A and ↓ Eotaxin & IL-10 mRNA levels in Long COVID sera vs controls.

04. Trend toward lower MoCA scores with higher inflammation.

BACKGROUND

Long COVID (LC) is characterized by cognitive symptoms that persist beyond 12 weeks after SARS-COV2 infection, yet its biological basis remains unclear.

Sustained inflammation is a leading hypothesis for these persistent cognitive deficits.

AIM: Examine **peripheral inflammatory markers and brain glucose metabolism** to explore the mechanisms behind cognitive Long COVID.

METHODS

Cross-sectional study of **two Argentine Long-COVID cohorts** with persistent cognitive complaints and no prior neurological disease. All participants underwent:

- **Cognitive screening:** MoCA, normalised to UDS3 reference data

- **Blood cytokines:** Multiplex ELISA for 9 markers: eotaxin, IFN- γ , IL-1 β , IL-4, IL-6, IL-10, IL-17A, MCP-1, TNF- α

- **Brain FDG-PET:** Analysed by UNSAM team with two independent pipelines (in-house & Neurocloud); multi-site data harmonised with ComBat.

Only regions with **consistent hyper- or hypometabolism across both pipelines** were retained. MoCA–cytokine correlations were explored.

RESULTS

62 Long-COVID participants (38 F; age 52 ± 12 ; MoCA $z = -0.5 \pm 1.4$) — **49 with FDG-PET**, assessed **20 ± 11.5 months post-infection**.

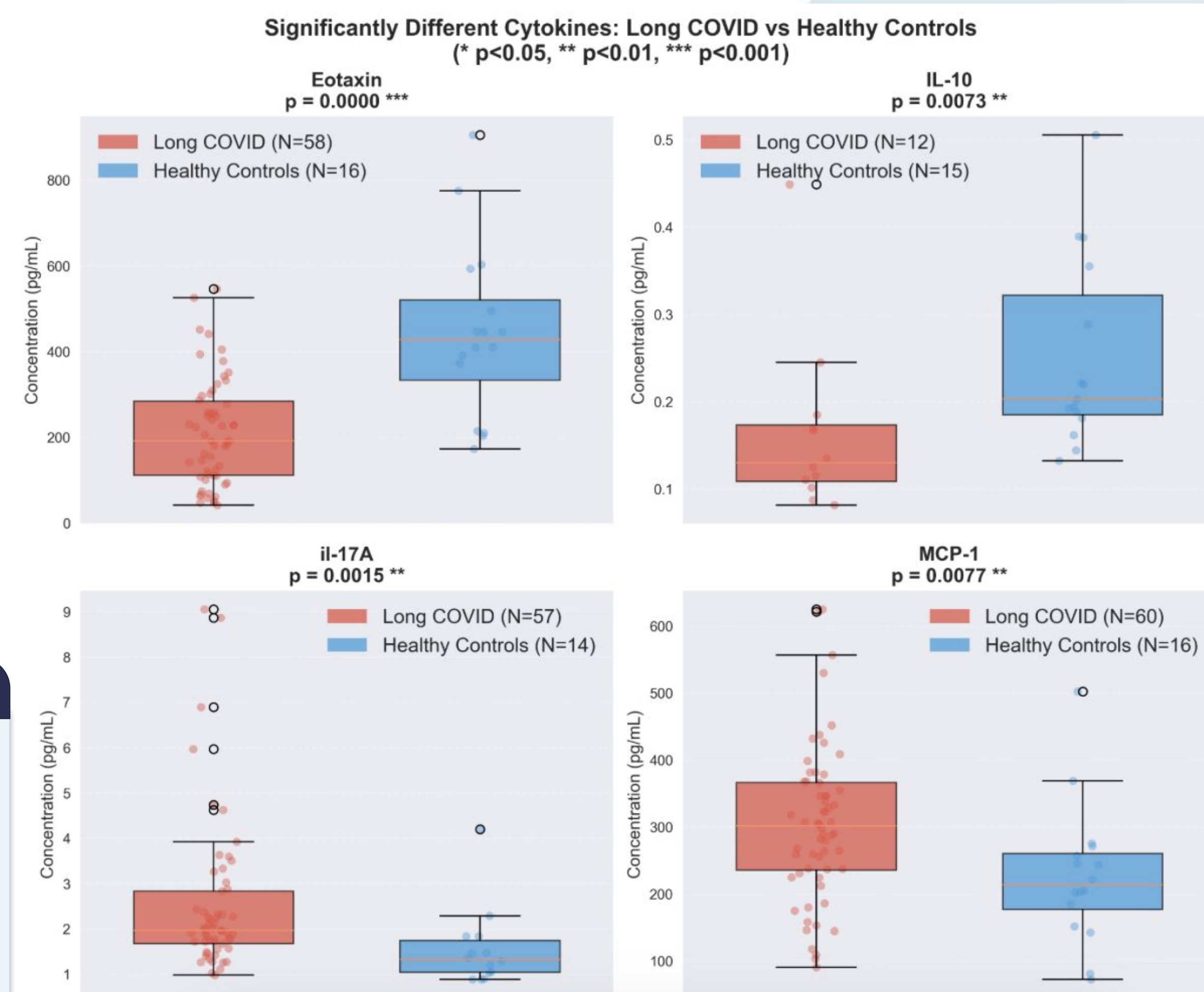
Top complaints: concentration 91% · memory 87% · attention 74% · fatigue 69%.

- Consistent **hypermetabolism in bilateral frontal & parietal cortices** (Table 1).
- ↑ **MCP-1 and IL-17A** · ↓ **Eotaxin and IL-10** vs controls (Figure 1).
- Weak negative MoCA correlations: MCP-1 ($r = -0.25$, $p = 0.06$), IL-17A ($r = -0.25$, $p = 0.05$).

Table 1. Brain regions with significant FDG-PET differences (Long COVID vs controls) concordant across both pipelines — all hypermetabolic (HYPER). Z-scores and p-values from the in-house and Neurocloud pipelines.

Anatomical Region	Hemisphere	Effect Direction	Z-score (Neurocloud)	p-value (Neurocloud)	Z-score (In-house)	p-value (In-house)
Superior frontal gyrus	L	HYPER	2.45	0.014	2.31	0.019
Superior frontal gyrus	R	HYPER	2.6	0.01	2.4	0.015
Anterior cingulate cortex	L	HYPER	2.3	0.018	2.1	0.03
Anterior cingulate cortex	R	HYPER	2.15	0.025	2.05	0.034
Inferior parietal lobule (supramarginal/angular)	L	HYPER	2.75	0.006	2.51	0.012
Inferior parietal lobule (supramarginal/angular)	R	HYPER	2.4	0.015	2.3	0.021
Middle frontal gyrus	L	HYPER	2.1	0.032	2.2	0.027
Inferior frontal gyrus (Broca area)	L	HYPER	2.35	0.017	2.18	0.029
Inferior frontal gyrus (Broca area)	R	HYPER	2.2	0.026	2.12	0.033

Figure 1. Cytokines elevated (IL-17A, MCP-1) and decreased (Eotaxin, IL-10) in Long COVID vs healthy controls. Kruskal–Wallis tests; p-values above each panel.



CONCLUSIONS

- Long COVID shows **frontal hypermetabolism** and **immune dysregulation**.
- Low IL-10 and high MCP-1/IL-17A suggest a **pro-inflammatory state**.