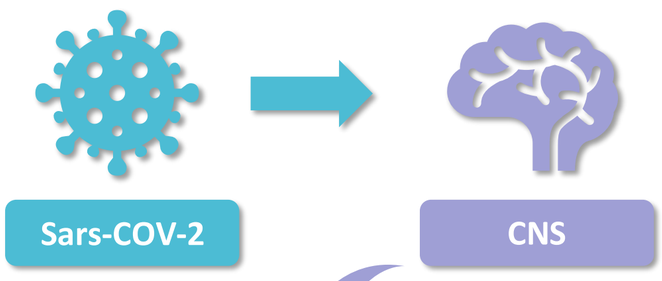
Neuroinflammatory Signatures and Prefrontal Mechanisms in Long COVID: Insights from 7T MRI and Cognitive Testing

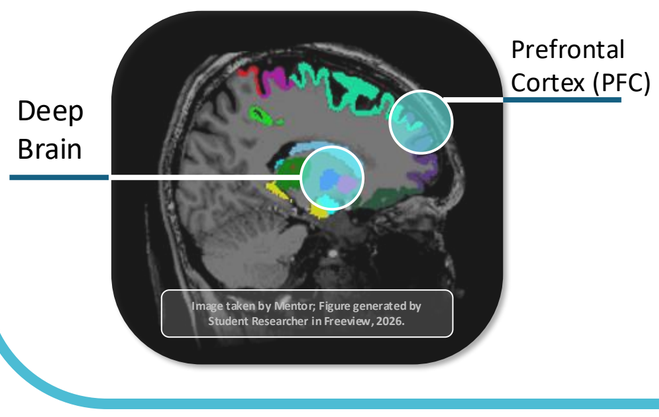
INTRODUCTION

- Fatigue
- Loss of taste/smell
- Brain fog

Developed **long-term neurological symptoms**[1] — **56% of COVID patients**

NeuroPASC
Long term *neurological* effects of COVID-19





Direct viral invasion of CNS, **blood-brain barrier disruption**, microglial/astrocyte activation[2,3]

OBJECTIVES

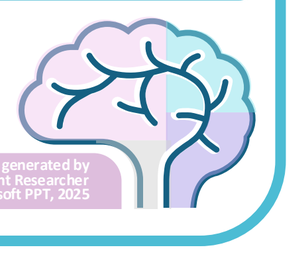
- **Phase 1** — Compare cortical thickness and subcortical volume measurements across NeuroPASC subgroups
- **Phase 2** — Compare brain health in COVID-19 with other neurological disorders using brain age
- **Phase 3** — Investigate the relationship between prefrontal cortex morphology and cognitive performance

DATA COLLECTION

- 47 COVID Patients
- 36 Post-Pandemic Controls
- 69 Pre-Pandemic Controls

7T MRI

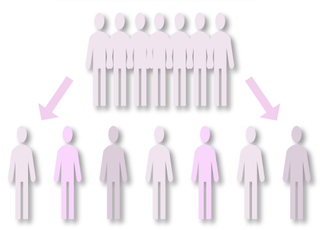
FreeSurfer 7 Segmentation



METHODS

PHASE 1
Subcortical volumes and cortical thickness vs. symptom subgroups

All Subjects → Subgroups



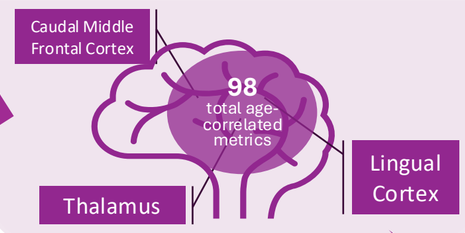
- Depression
- Anxiety
- Brain Fog
- Fatigue
- Balance Issues
- Impaired Taste
- Impaired Smell

GLM with age and sex as controlled covariates

PHASE 2
Quantify brain age as a measure of brain health

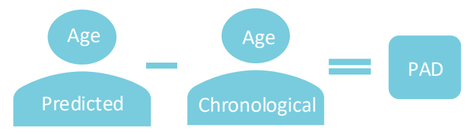
Linear Regression: Chronological Age vs. Brain Metrics

Select Age-Correlated Brain Regions



Model trained on **age-correlated regions and ratios** in **pre-pandemic controls.** Provides **age prediction for each region.**

Brain Predicted Age Deficit (PAD)



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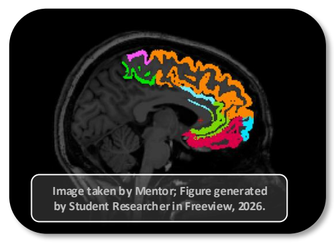
PHASE 3
Associate objective neuropsychological test scores with PFC regions

COVID Patients + Controls

- Wide Range Achievement
- Phonemic Fluency
- Semantic Fluency
- Hopkins Verbal Learning Test

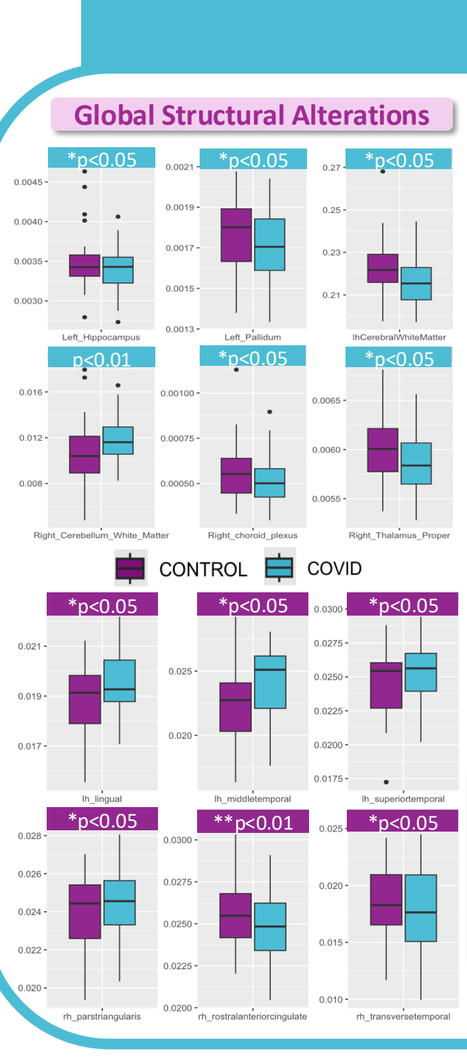
The neuropsychological tests assess **intellectual functioning, verbal flexibility, verbal memory and semantic memory**



Associations performed between **neuropsychological test scores and PFC regional measurements**

RESULTS

Global Structural Alterations



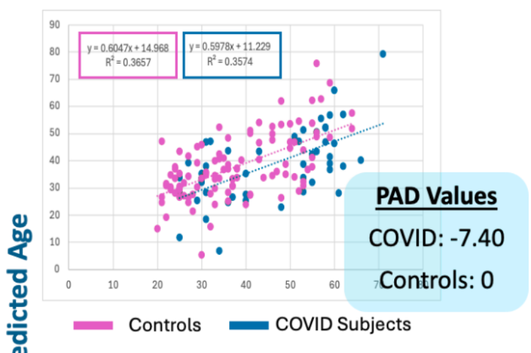
Reduced choroid plexus and ventricle volume suggests compromised blood-brain barrier and CSF

Lower brain volumes and higher cortical thicknesses compared to healthy controls

Altered structures align with symptoms

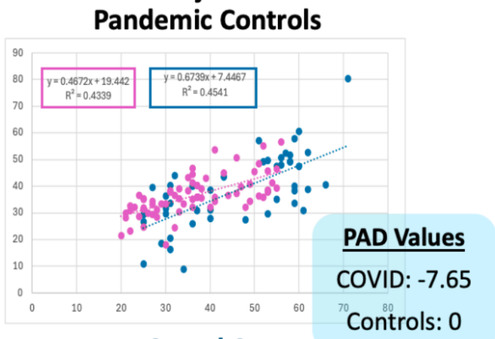
Figure generated by Student Researcher in R, 2025

Predicted Brain Ages



PAD Values
COVID: -7.40
Controls: 0

COVID Subjects vs. Pre-Pandemic Controls



PAD Values
COVID: -7.65
Controls: 0

COVID patients show "younger" brain ages

Figure generated by Student Researcher in Excel, 2025

NeuroPysch Test Scores

	HVLT_Immediate	HVLT_Delay
COVID	-0.336043386	-0.533945122
Control	-0.18530831	-0.370658376
P-Value	0.288343884	0.28155983
	HVLT Recognition	**WRAT**
COVID	0.088964823	113.6976744
Control	0.218965984	108.7714286
P-Value	0.27621357	0.090726306
	Trails A	**Trails B**
COVID	-1.305712154	-0.382387706
Control	-0.823777675	-0.422989989
P-Value	0.101146397	0.442228856
	Semantic Fluency	**Phonemic Fluency**
COVID	-0.515058242	-0.314225713
Control	-0.455888161	-0.055508319
P-Value	0.391622017	0.143091171

PFC Structural Alterations

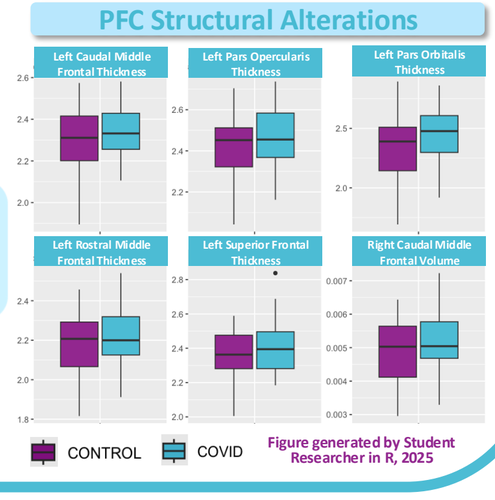


Figure generated by Student Researcher in R, 2025

CONCLUSION

- Identified unique neuroinflammatory signature never observed before
- Revealed hidden compensatory mechanisms maintaining function
- Established potential blood-brain barrier compromise (choroid plexus)
- Demonstrated failure of traditional brain age assessment tools

References

Cited

1. Romero-Sánchez et al. (2020). *Neurology*, 95(8).
2. Farhadian et al. (2023). *JAMA Network Open*, 6(11).
3. Kanberg et al. (2020). *Neurology*, 95(12).

Not Cited

4. Douaud et al. (2022). *Nature*, 604.
5. Nath & Spudich (2022). *Science*, 375.
6. Kesler et al. (2024). *MedRxiv*.
7. Mohammadi-Nejad et al. (2024). *MedRxiv*.
8. Verma et al. (2022). *Epilepsy & Behavior Reports*.

J. Desai