

Structural Brain Differences after Infection with various SARS-CoV-2 Variants of Concern

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Background

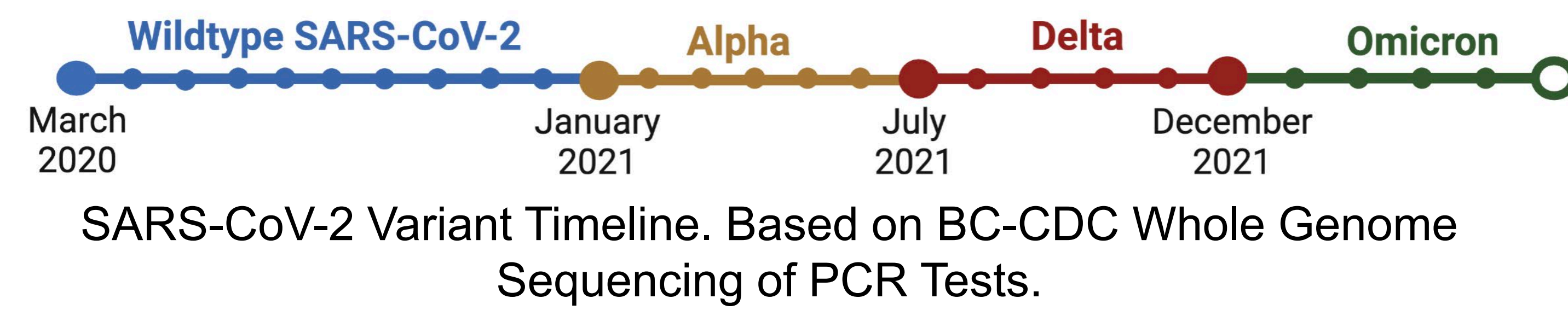
- Since the beginning of the COVID-19 pandemic, several SARS-CoV-2 Variants of Concern (VoCs) have evolved.
- In Canada, the predominant VoCs have been the Alpha, Delta and Omicron variants.
- Past research has found higher hospitalization rates¹ and longer recovery times associated with the Delta variant.²
- COVID-19 illness has been associated with differences in white matter diffusivity, with more pronounced effects with a more severe acute COVID-19 illness.^{3,4}

Objectives & Hypotheses

- We aimed to compare the white matter microstructure of the brain differentially across SARS-CoV-2 variants.
- We hypothesized that the Delta variant would have white matter diffusivity metrics that indicate worsened white matter integrity, when compared to Wildtype SARS-CoV-2.

Methodology

- Participants were recovered COVID-19 patients 6 months post-acute illness.
- VoC classifications were based on BC-CDC data:



- Participants underwent Magnetic Resonance Imaging (MRI) with Diffusion Tensor (DTI) to assess brain structure.
- Four DTI metrics (AD, FA, MD, RD) were compared using Tract-Based Spatial Statistics (TBSS) with 2000 permutations.
- Analyses were covaried for age, sex, BMI and years of education.

Results

- Wildtype SARS-CoV-2 (n=36), the Alpha variant (n=27), and the Delta variant (n=20) groups were similar on demographic and clinical features including age, sex, hypertension, and hospitalization for acute COVID-19 (Figure 1).
 - The Delta group had more vaccine doses before acute COVID-19 than Wildtype SARS-CoV-2 and the Alpha variant ($p < 0.001$).
- The Delta variant had lower FA and higher AD, MD, and RD than Wildtype SARS-CoV-2 (Figure 2) and the Alpha variant (Figure 3).

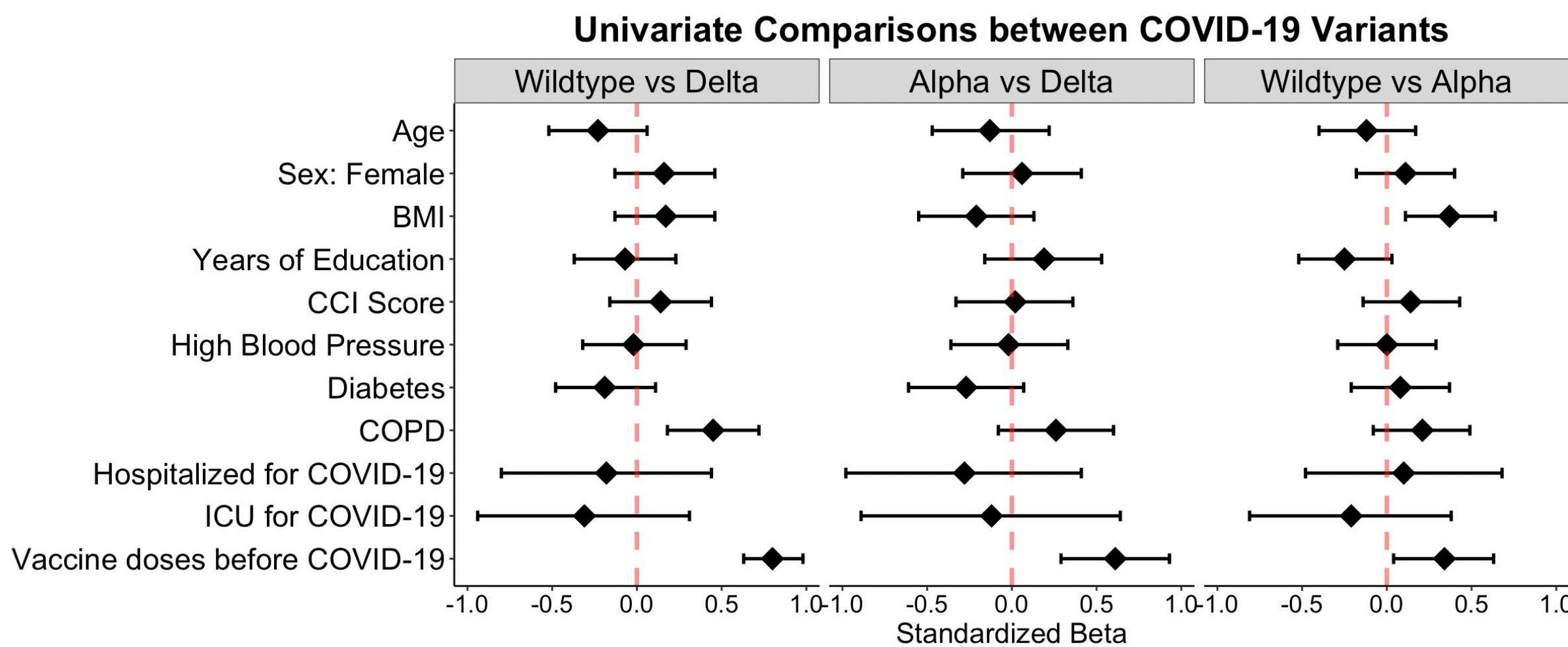


Figure 1. Forest plot of univariate differences between SARS-CoV-2 variant groups on demographic and clinical variables. The standardized beta of the difference between groups is plotted with a 95% confidence interval.

Wildtype SARS-CoV-2 vs Delta variant

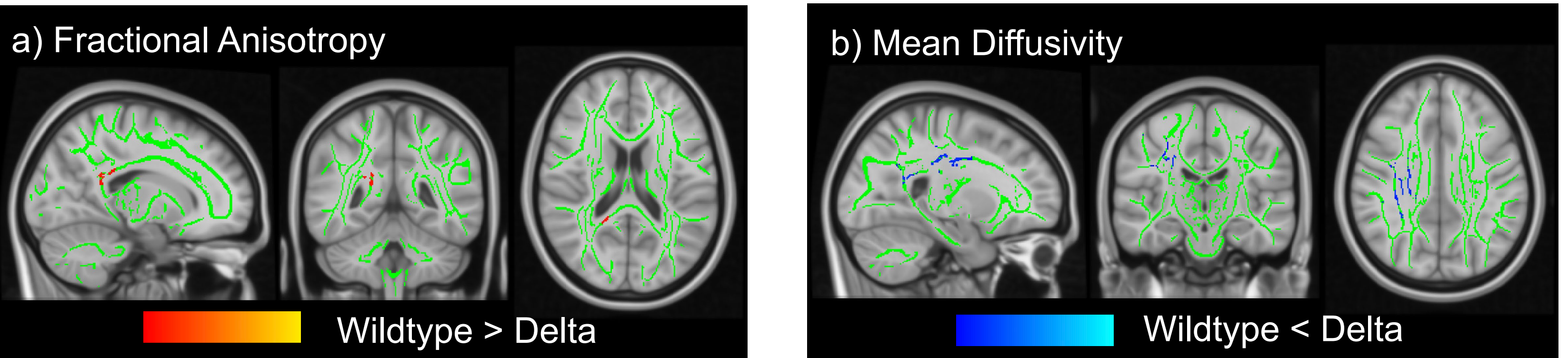


Figure 2. TBSS results comparing Wildtype SARS-CoV-2 to the Delta variant on a) FA and b) MD. Green regions represent the white matter skeleton. Red-Yellow voxels represent regions where Wildtype SARS-CoV-2 was significantly greater than the Delta variant. Blue voxels represent regions where Wildtype SARS-CoV-2 was significantly lesser than the Delta variant.

Alpha variant vs Delta variant

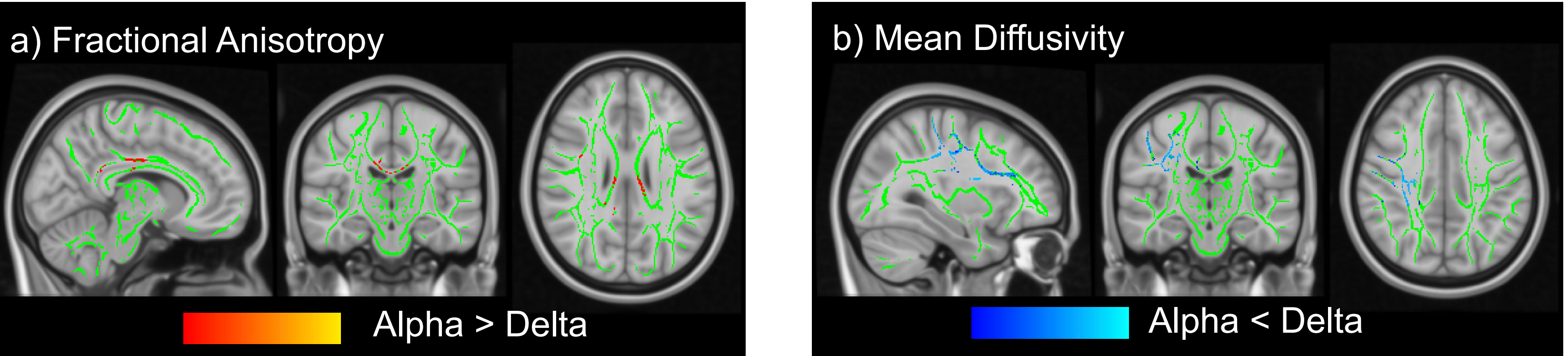


Figure 3. TBSS results comparing the Alpha variant to the Delta variant on a) FA and b) MD. Green regions represent the white matter skeleton. Red-Yellow voxels represent regions the Alpha variant was significantly greater than the Delta variant. Blue voxels represent regions where the Alpha variant was significantly lesser than the Delta variant.

	Number of voxels (p_{min} ; p_{max})	
DTI Metric	Wildtype vs Delta	Alpha vs Delta
FA	1 934 (0.028; 0.0495)	12 598 (0.014; 0.0495)
AD	106 (0.045; 0.049)	3 790 (0.003; 0.0475)
MD	616 (0.0415; 0.0495)	12 256 (0.003; 0.0435)
RD	1 352 (0.0405; 0.0495)	15 860 (0.008; 0.048)

Table 1. Number of significant voxels for TBSS results between Wildtype SARS-CoV-2 and the Delta variant and the Alpha variant and the Delta variant.

Discussion

- Infection with the Delta variant may have differential effects on white matter structure in the brain, compared with Wildtype SARS-CoV-2 and the Alpha variant.

Limitations & Future Directions

- VoC categorization was not based on genome sequencing of PCR tests, therefore some participants may have been inaccurately categorized.
- We are in the process of cross-validating these results with larger cohorts.
- Longitudinal follow-up of our participants at future timepoints is required to determine whether this effect is specific to the timepoint examined or persistent.

Acknowledgements

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References

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2. Kumar, Nitya, et al. "COVID-19 recovery patterns across alpha (B. 1.1. 7) and delta (B. 1.617. 2) variants of SARS-CoV-2." *Frontiers in immunology* (2022): 379.
3. Douaud, Gwenaëlle, et al. "SARS-CoV-2 is associated with changes in brain structure in UK Biobank." *Nature* 604.7907 (2022): 697-707.
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