Does COVID-19 Infection Accelerate Age-Related Cognitive Decline?

BACKGROUND. Similar neuroimaging abnormalities are reported in post-COVID patients and patients with AD. Moreover, COVID-19 and Alzheimer's Disease (AD) share genetic vulnerabilities and have similar cognitive symptoms of COVID (e.g., memory impairment, mental fatigue, anosmia, etc.). These findings raise the concern that COVID infection may increase the risk that older patients will develop Alzheimer's disease.

METHOD. Self-reported COVID histories were recorded from 415 older participants (mean age 70.1 years), including 310 participants longitudinally tested beginning in 2022. The effects of COVID on cognitive performance were assessed with 32 computerized subtests of the California Cognitive Assessment Battery (CCAB). Omnibus z-scores were averaged over 70 test measures at enrollment, and again at 6-month and 18-month post-enrollment in the 310-participant sample.

RESULTS. Significant demographic differences were seen between COVID+ and COVID- groups (Table 1). COVID+ patients performed worse than COVID- patients overall (Figure 1, $t(85) = -2.80, p<0.01$) and when analyzed with a conventional model using Age, Education, and Gender (AEG) as regressors ($t(85) = -3.07, p<0.005,$ Figure 2). However, inter-group differences failed to reach significance ($t(85) = -0.97, NS$) when analyzed with a comprehensive 15-factor model that factored out additional demographic influences including vocabulary, comorbidities, depression, anxiety, functional status, and race. In contrast, COVID infection severity (estimated from augmented WHO scores) correlated significantly with omnibus z-scores when analyzed with the comprehensive model ($r = -0.30, t(64) = -2.52, p<0.02$) but correlations failed to reach significance when analyzed with the conventional (AEG) model.

The effect of incidental "breakthrough" COVID infections in participants (97.35% were vaccinated prior to retest) was analyzed at 6-months (38 cases) and 18-months (50 cases). Breakthrough infections prior to 6-month retest were paradoxically associated with improved 6-month Omnibus scores ($t(49) = 2.74, p < 0.01$), while no significant differences were observed for breakthrough infections prior to 18-months ($t(90) = 0.95, NS$).

CONCLUSION. These preliminary results suggest that infections with Wild Type and Delta variants early in the COVID pandemic produced cognitive deficits, particularly among patients hospitalized with COVID. In contrast, post-inoculation breakthrough infections caused no significant decline in cognitive performance.

	n	Age	Male%	White	GAD7	GDS	EDU	fs20	OMNI
COVID-	352	70.47	53%	65%	1.93	1.77	16.07	4.50	0.05
COVID+	63	68.05	35%	32%	3.43	2.59	13.22	5.24	-0.29

Table 1. Demographic characteristics of participants. The 63 COVID+ participants at enrollment were younger, more often female, more often from racial minorities (White = percent Caucasian), had higher anxiety (GAD7), depression (GDS), and functional status (FS20) scores, and had less education (EDU) than COVID- participants (all $p < 0.05$). Their unadjusted performance scores, averaged over all subtests (OMNI), were also significantly below those of COVID- participants ($p<0.01$, Figure 1).

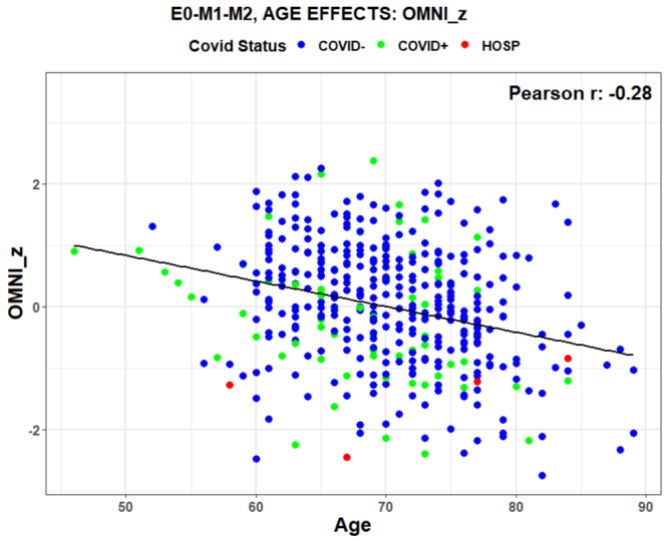

FIGURE 1. Unregressed omnibus z-scores as a function of age. Data points show COVID-19 status (blue = COVID-, green = COVID+, red = Hospitalized with COVID). The regression line shows a normal decline in performance with age. Data from 415 participants. E0-M1-M2 refers to the three test sessions that were included in the average.

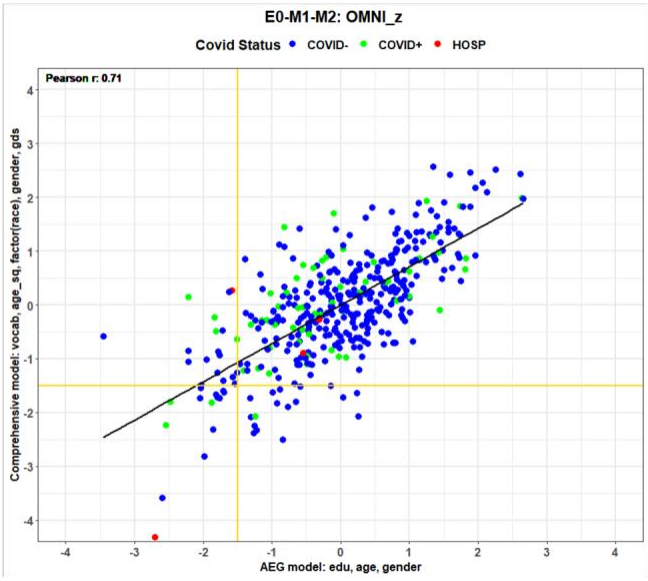

Figure 2. Omnibus z-scores from enrollment tests calculated with comprehensive and AEG regressors. Axis labels show significant predictors in order of significance (e.g., vocabulary was the most significant predictor in the Comprehensive model). Covid status is coded by dot color.