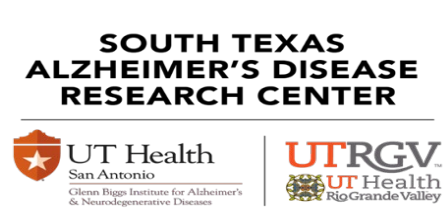


Multidomain Cognitive Performance in COVID-19 and Illness Controls Compared to Healthy Controls



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COVID-19 is associated with poorer executive function and verbal memory performance

INTRODUCTION

Persistent cognitive symptoms following COVID-19 infection have emerged as a major clinical and public health concern.

Understanding whether cognitive impairment varies by COVID-19 severity and how it compares with non-COVID illness is critical for early identification and informing targeted interventions.

METHODS

This cross-sectional study was conducted within the 7T NeuroCOVID Consortium, an international, multi-site cohort including The University of Texas Health Science Center at San Antonio, Houston Methodist Research Institute, The University of Pittsburgh, Nottingham University, and Massachusetts General Hospital.

COVID-19 status was determined by structured self-report categorized as COVID-19 survivors, healthy controls, or illness controls, (COVID-19-like symptoms with non-COVID infection). Acute COVID-19 severity was classified according to World Health Organization criteria (mild, moderate, severe, or critical).

Participants completed the Uniform Data Set (UDS-3) neuropsychological battery ≥6 months after infection. Primary outcomes included executive function, attention/processing speed, and verbal learning and memory measures.

Multivariable linear regression models were used to compare cognitive performance between groups and to evaluate trends across COVID-19 severity levels, adjusting for age, sex, education, and study site.

Statistical significance was set at false discovery rate corrected $\alpha=0.05$

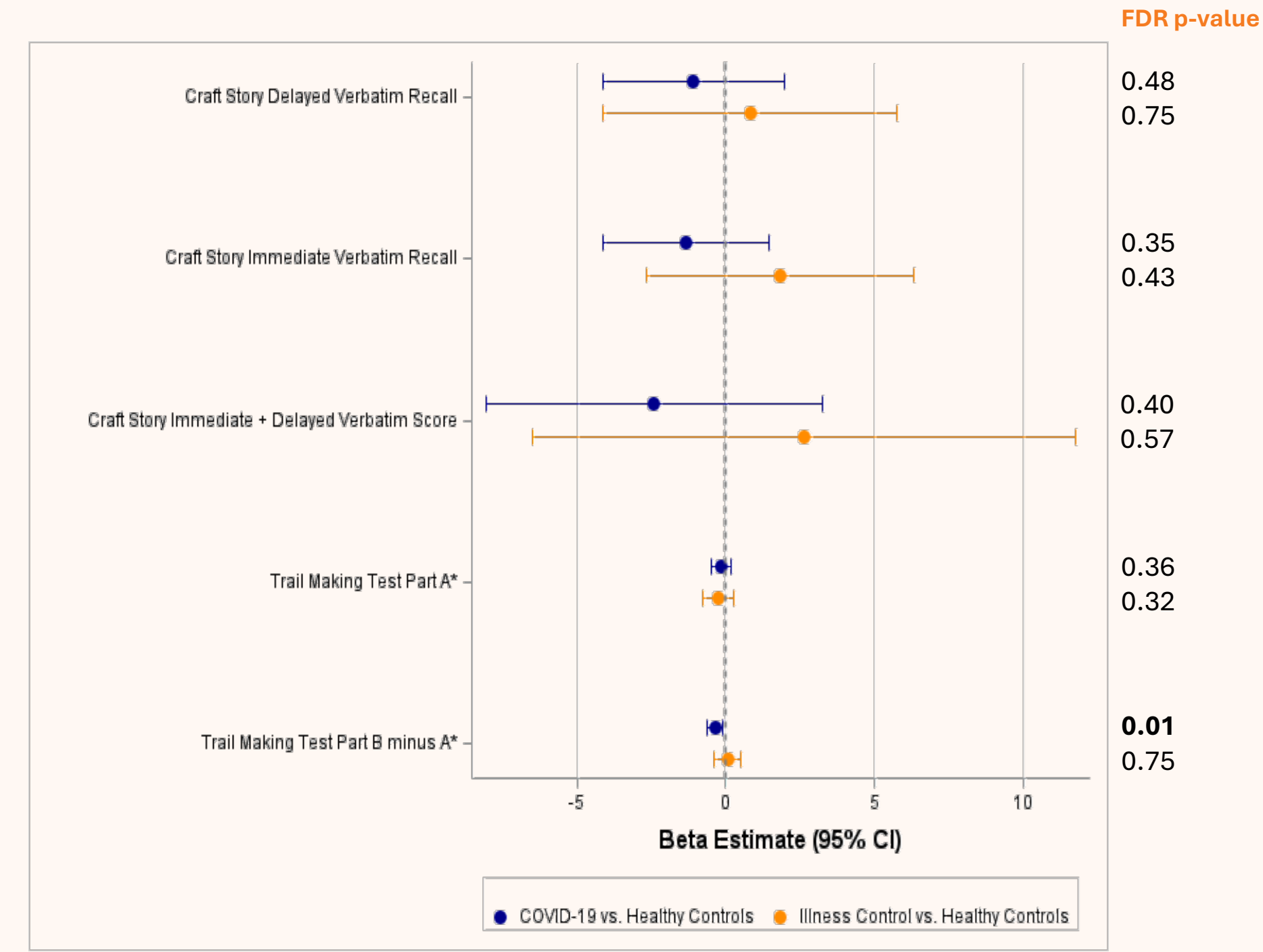
RESULTS

Table 1. Participants Characteristic

Characteristic	Overall	COVID-19	Healthy Controls	Illness Controls
N	183	138	32	13
Age, years	61.21 (8.5)	60.64 (8.4)	63.91 (8.9)	60.69 (7.6)
Female	101 (55.5)	74 (53.6)	21 (65.6)	6 (50.0)
Education				
High School Degree or Some College	77 (42.3)	60 (43.8)	11 (34.4)	6 (46.2)
Bachelor's Degree	56 (30.8)	41 (29.9)	10 (31.3)	5 (38.5)
Doctorate or master's degree	49 (26.9)	36 (26.3)	11 (34.4)	2 (15.4)
Self-reported ancestry				
Hispanic or Latino	34 (18.6)	27 (19.6)	5 (15.6)	2 (15.4)
Non-Hispanic White	106 (57.9)	76 (55.1)	20 (62.5)	10 (76.9)
Black or African American	27 (14.8)	22 (15.9)	5 (15.6)	0
other	16 (8.7)	13 (9.4)	2 (6.3)	1 (7.7)
COVID-19 Severity				
Mild	64 (35.0)	63 (45.7)	n/a	1 (7.7)
Moderate	20 (10.9)	20 (14.5)	n/a	n/a
Severe	41 (22.4)	41 (29.7)	n/a	n/a
Critical	14 (7.7)	14 (10.1)	n/a	n/a
Hospitalized	72 (48.7)	63 (46.7)	n/a	9 (69.2)
ICU	23 (16.7)	21 (16.7)	n/a	2 (16.7)
Site				
UTHSA	46 (25.1)	37 (26.8)	9 (28.1)	0
Houston	57 (31.1)	41 (29.7)	10 (31.3)	6 (46.2)
Pittsburgh	34 (18.6)	28 (20.3)	1 (3.1)	5 (38.5)
Nottingham	46 (25.1)	32 (23.2)	12 (37.5)	2 (15.4)
Craft Story Delayed Verbatim Recall, score*	17.91 (7.13); 17.00 [13.00, 23.00]	17.57 (7.43); 16.00 [13.00, 22.50]	19.18 (5.89); 19.50 [13.50, 24.00]	18.62 (6.51); 20.00 [15.00, 23.00]
Craft Story Immediate Verbatim Recall, score*	20.32 (6.55); 20.00 [16.00, 25.00]	19.87 (6.68); 19.00 [16.00, 24.00]	21.46 (6.40); 21.00 [16.50, 27.00]	22.38 (4.99); 23.00 [21.00, 26.00]
Trail Making Test Part A, mins*	0.56 (0.30); 0.52 [0.38, 0.62]	0.58 (0.32); 0.53 [0.39, 0.67]	0.49 (0.14); 0.49 [0.38, 0.57]	0.56 (0.35); 0.48 [0.40, 0.55]
Trail Making Test Part B minus A, mins*	0.96 (0.76); 0.68 [0.47, 1.13]	17.91 (7.13); 17.00 [13.00, 23.00]	0.81 (0.84); 0.61 [0.35, 0.93]	0.62 (0.37); 0.58 [0.40, 0.70]

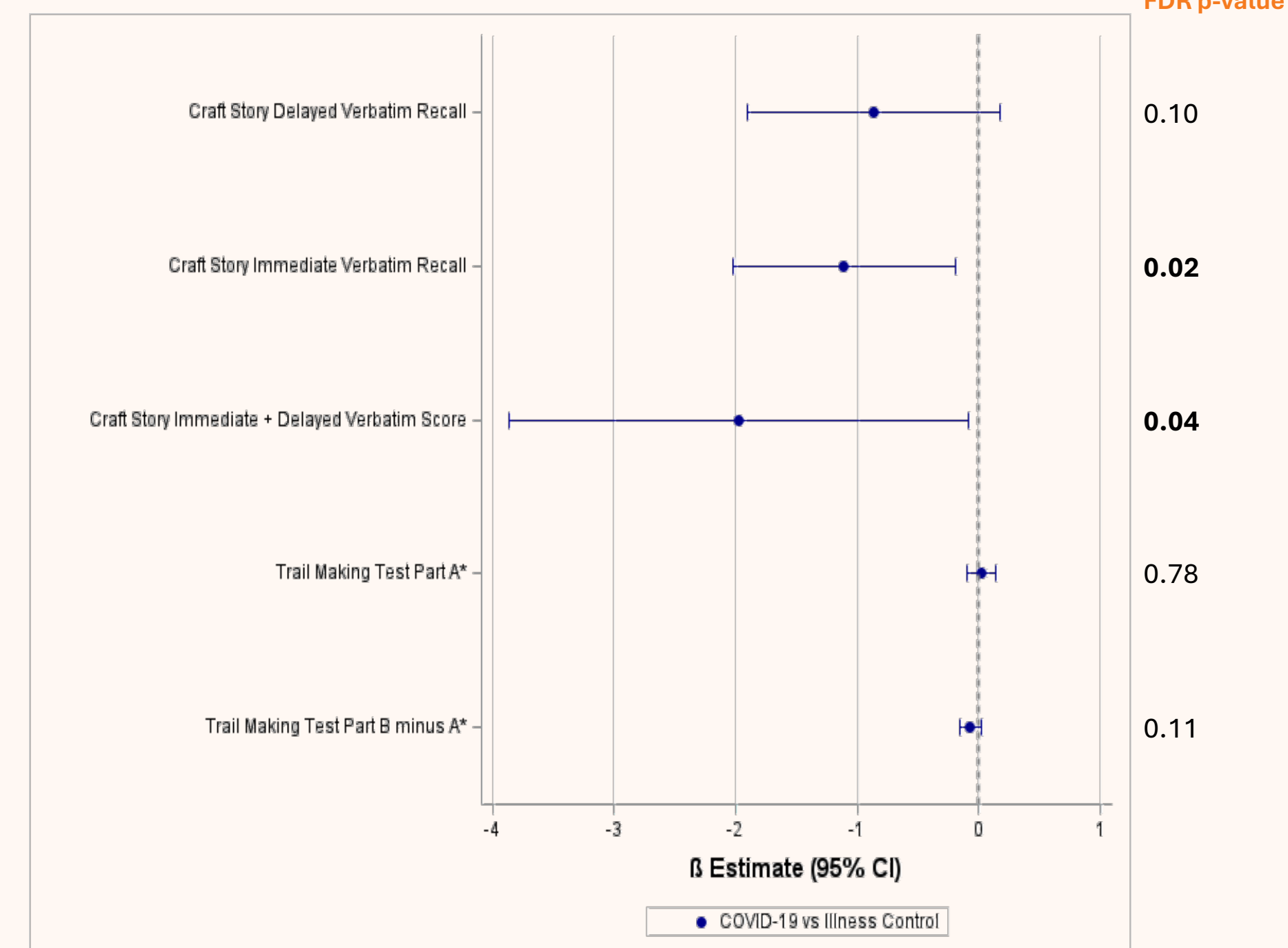
Numbers are reported as n(%), unless otherwise stated. *mean (SD); Median [Q1, Q3]
Abbreviations: Coronavirus disease 2019 (COVID-19); Intensive care unit (ICU); University of Texas Health at San Antonio (UTHSA)

Figure 1. Associations Between COVID-19 Status and Cognitive Performance



*Natural log transformed to normalize distribution and directionality adjusted so that higher scores consistently indicates better performance.

Figure 2. Cognitive Performance in COVID-19 Survivors Compared with Illness Controls



*Natural log transformed to normalize distribution and directionality adjusted so that higher scores consistently indicates better performance.

COVID-19 infections were associated with lower scores in executive function and memory several months after infection. The observed pattern of results shares features with cognitive profiles seen in early neurodegeneration and vascular conditions, suggesting overlapping or convergent mechanisms. These findings highlight the need for longitudinal studies to clarify trajectories of cognitive recovery and to identify opportunities for early intervention in COVID-19 survivors.

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