Cognitive, Motor, & Negative Valence Systems in Neurologic PASC: A Preliminary Study

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Background

- Our goal was to apply the **Research Domain Criteria** (RDoC) framework to better characterize neuropsychiatric alterations in individuals with neuro-PASC
- **Neurologic post-acute sequelae of COVID-19** (Neuro-PASC): New or worsened neurologic and/or psychiatric symptoms present 3 months after COVID-19 lasting for more than 2 months

Methods

- Neuro-PASC participants were referred from Yale's NeuroCOVID Clinic; Never-COVID controls were recruited from New Haven, CT and Baltimore, MD (**Table 1**)
- Participants completed questionnaires and tasks assessing the cognitive, positive valence (PV), negative valence (NV), motor, and social processing systems (**Figure 1**)
- 11 participants underwent a **3T MRI** with diffusion tensor imaging to explore white matter integrity (global white matter fractional anisotropy [FA])
- Neuro-PASC alterations were examined using ANCOVAs. Covariates included: biological sex, race/ethnicity, age, and years of education

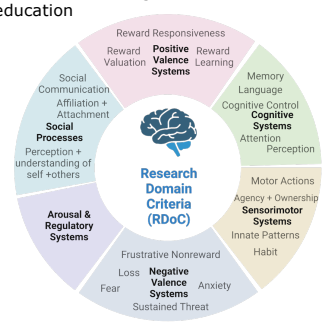
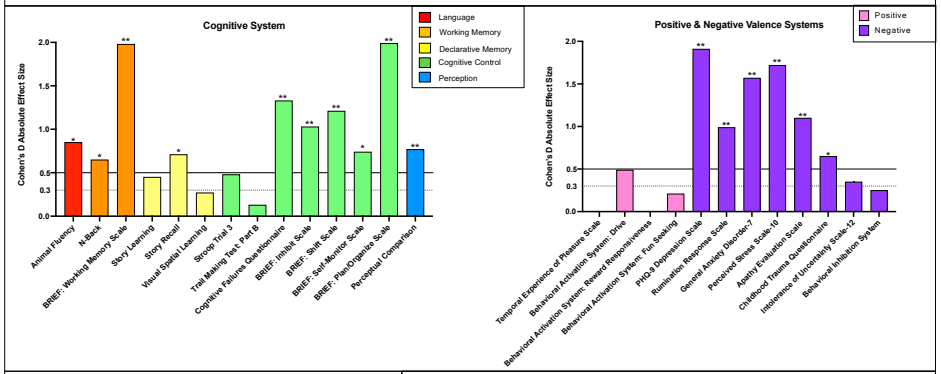


Figure 1. Research Domain Criteria An NIH research framework for investigating mental disorders

Neuro-PASC is associated with alterations in cognitive, motor, and negative valence RDoC systems

Figure 2. RDoC Systems Self-reported and objective-based performance on an RDoC battery presented as standardized absolute effect size differences (Cohen's *D*) between neuro-PASC and control groups (** $p<0.01$, * $p<0.05$)



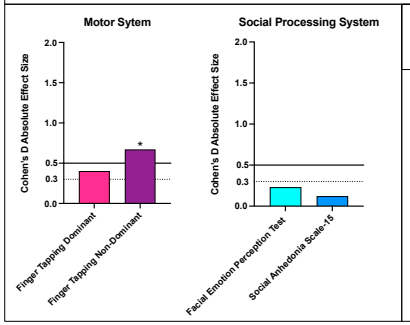


Figure 3. 3T MRI A) An axial fractional anisotropy map; B) DTI global white matter FA values for a subset of Neuro-PASC and control participants plotted against time from illness

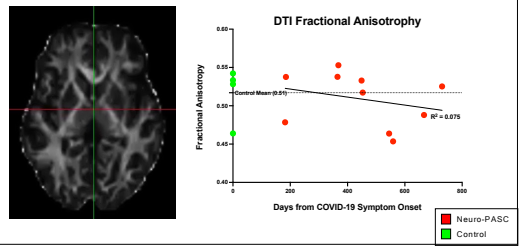


Table 1. Demographics

Enrollment Characteristics	Neuro-PASC (n=25)	Control (n = 29)	p-value
Age (Median, IQR)	43 (36 – 51)	35 (31 – 46)	0.19
Race/Ethnicity			0.05*
White	92%	67%	
Black	8%	11%	
Asian	0%	22%	
Hispanic	8%	11%	0.99
Female Gender	76%	78%	0.99
Education (years)	16 (14 – 17)	17 (14 – 17)	0.80
Comorbidities			
Alcohol	0%	0%	
Smoking	8%	22%	0.22
Hypertension	20%	0%	0.29
Type 2 Diabetes	0%	0%	
Obesity	8%	0%	0.99
Antidepressant Use	28%	22%	0.99

Acute COVID-19 Illness	Neuro-PASC (n = 25)
Days between symptom onset and research visit	402 (269 – 523)
Vaccination Status	
Vaccinated	8%
Unvaccinated	92%
Acute Illness Level of Care	
Home	92%
Hospital Floor	4%
ICU	4%
Neuro-PASC Symptoms	
Fatigue	95%
Cognitive Impairment	91%
Anxiety/Depression	82%
Headache	73%
Neuropathy	68%
Vertigo/Dizziness	68%
Dysautonomia	68%
Poor Sleep	64%
Shortness of Breath	59%
Weakness	59%
Off Balance/Falls	59%
Post-Exertional Malaise	59%
Vision Changes	36%
Nausea/Vomiting	36%
Anosmia/Ageusia	32%

Results

- Neuro-PASC group performed worse in language, working memory, declarative memory, and perception (**Figure 2**)
- Neuro-PASC group reported greater cognitive control difficulties (e.g., behavioral inhibition, set shifting) without demonstrating alterations on performance-based metrics (Stroop, Trail Making Test-Part B)
- Neuro-PASC group had slower motor function, but there were no differences in PV and social processing domains
- Neuro-PASC group reported more NV issues, including greater depression, rumination in response to depressive mood, apathy, childhood trauma, anxiety, and perceived stress (**Figure 2**)
- In a subset of Neuro-PASC participants who underwent MRI, there was a dynamic range of FA values with a mean of 0.509 (IQR 0.481 – 0.536) (**Figure 3**)

Conclusions

- Previous studies of individuals with neuro-PASC have demonstrated impaired executive functioning, processing speed, attention, category fluency, memory encoding, and verbal fluency[1,2]; We found similar alterations in the RDOC cognitive system
- Novel alterations were observed in motor and NV systems, which warrant additional investigations
- In the future, we plan to examine white matter integrity as a pathophysiologic contributor to the alterations in RDoC systems

No Disclosures

Funding: R01 MH125737-02S1; Merck Investigator Studies Program; K23 MH118899; R01 AI57488; T32NS105583-04

Acknowledgements: Thank you to all participants

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