Inflammatory and Cognitive Effects of COVID-19 Infection in Schizophrenia

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Background

- The role of viral infections in the pathophysiology of schizophrenia spectrum disorders (SSD) appears largely mediated by inflammatory cytokines, which are elevated in individuals with SSD
- Several inflammatory cytokines modulate the kynurenine pathway (KP), which breaks down tryptophan (TRP) into kynurenic acid (KYNA) and other products
- Elevated KYNA is thought to contribute to cognitive impairments in SSD and is identified as a biomarker of severe COVID-19 infection and long-COVID symptoms
- Individuals with SSD have been found to have increased antibody titers of other coronaviruses and have higher COVID-19 morbidity and mortality than other populations
- Literature on COVID-19 infection in SSD is focused on severe infection, with little known about the effects of mild to moderate COVID-19 infection on immune parameters, cognition and other clinical parameters in people with SSD

Study Methods

- We recruited 40 individuals with SSD diagnoses, aiming for half with prior COVID-19 and half without
- COVID-19 infection had to have occurred over 1 month before study participation and not more than 1 year before, without any related hospitalization
- Infection history was determined by testing records and/or self-report
- Participants completed a one-time visit that included:
  - MATRICS cognitive testing battery
  - Psychiatric symptom measures (SANS, BPRS)
  - Long-COVID symptom measures
  - Serum KYN, KYNA, TRP, cytokines, COVID antibodies, complete blood counts and complete metabolic panels
- Independent samples t-tests were used to examine differences in demographics, symptoms & antibodies between those with and without history of COVID-19
- Linear regression models (adjusted for age) were used to determine whether COVID-19 status predicted KP metabolite and cytokine levels

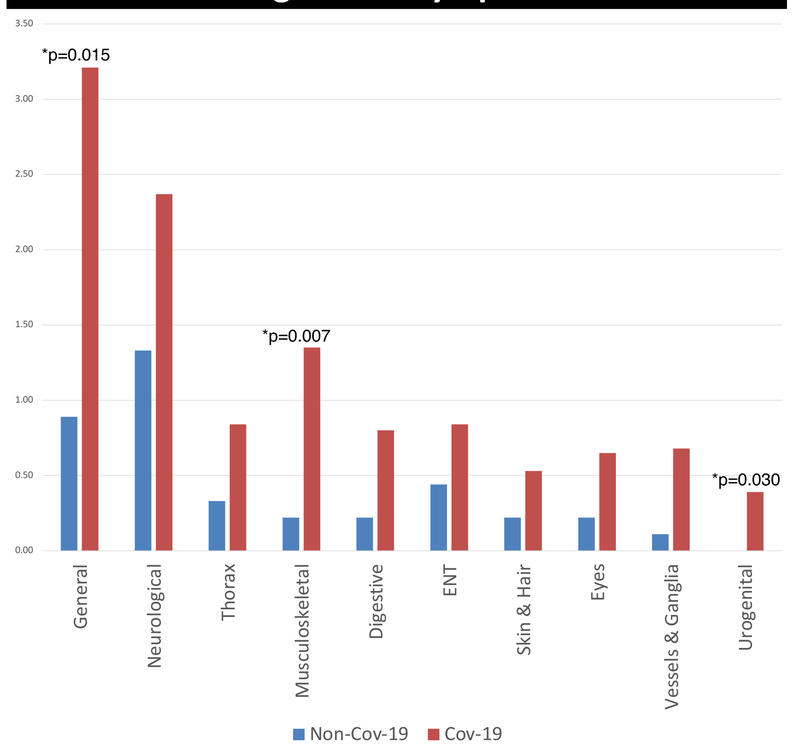
Infection History in COVID-19 Group (N=23)	
Total # cov-19 infections	1.22 (0.52)
Total # acute cov-19 symptoms	4.43 (3.55)
Total # long-covid symptoms	11.4 (13.9)
Days from most recent infection	310 (232)
Cov-19 status source info	Antigen test: 5 (21.7%) Self-report: 8 (34.8%) Combination: 10 (43.5%)

Acute cov-19 symptoms screened for: *fever, cough, dyspnea, fatigue, body aches, headache, anosmia, sore throat, congestion, nausea, diarrhea*

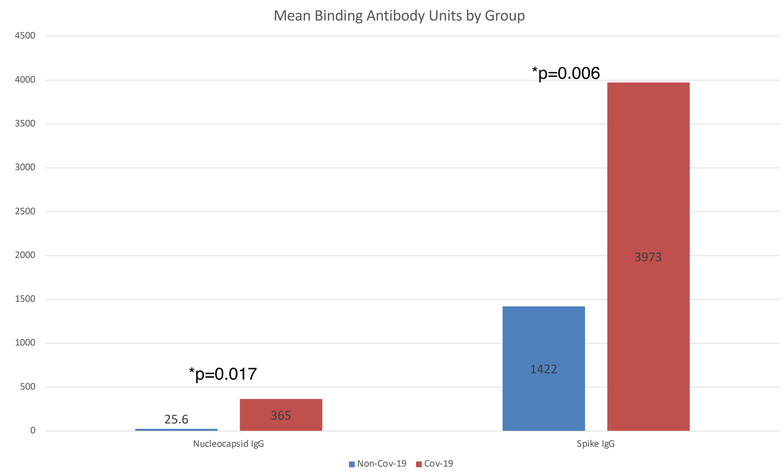
Demographic Information

	All N=40	Cov-19 N=23 (57.5%)	Non-Cov-19 N=17 (24.5%)	p-value
Age	41.9 (10.4)	40.4 (9.93)	43.8 (11.1)	0.333
Sex				
F	15 (37.5%)	8 (34.8%)	7 (41.2%)	0.934
M	25 (62.5%)	15 (65.2%)	10 (58.8%)	
Race:				
African American	27 (67.5%)	15 (65.2%)	12 (70.6%)	1.000
Asian	1 (2.5%)	1 (4.35%)	0 (0%)	
Caucasian	12 (30%)	7 (30.4%)	5 (29.4%)	
SSD Diagnosis:				
Schizoaffective	24 (60%)	15 (65.2%)	9 (52.9%)	0.648
Schizophrenia	16 (40%)	8 (34.8%)	8 (47.1%)	

Long-COVID Symptoms



Vaccination Status & Antibody Levels



	Vaccinated	Not Vaccinated
Non-Cov-19	16 (94.1%)	1 (5.88%)
Cov-19	20 (87%)	3 (13%)

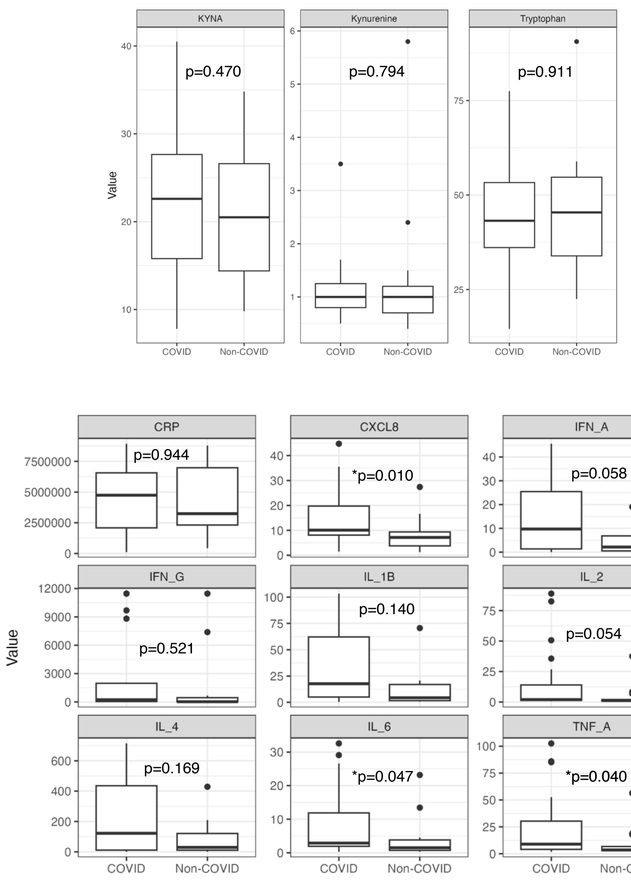
Cognitive & Symptom Outcomes

There were no significant differences between the non-COVID-19 and COVID-19 groups in:

- **Mean total BPRS score** (33.1 vs 34.0, p=0.790)
- **Mean total SANS score** (24.6 vs 24.7, p=0.983)
- **Mean overall MATRICS score** (32.7 vs 28.3, p=0.357) or in any MATRICS subdomain scores

History of COVID-19 was not significantly related to mean MATRICS overall and subdomain scores, including when adjusted for age, sex, education, vaccination status. COVID-19 antibody levels were not significantly related to MATRICS scores.

KP Metabolites & Cytokines



Anti-spike IgG antibody levels also predicted IL-6 levels (β=0.001, p=0.021) and IL-2 levels (β=0.002, p=0.018) when adjusted for age

Discussion

- In our population of individuals with SSD, those with a history of COVID-19 infection had more long-COVID symptoms
- Prior COVID-19 infection was related to elevations in TNF-alpha, IL-6, and CXCL8
- Anti-spike protein antibody levels were positively associated with IL-2 and IL-6 levels
- Prior COVID-19 infection was not significantly related to KP metabolites, psychiatric symptoms, or cognitive scores

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