BLOOD QUINOLINIC ACID AND KYNURENINE AS BIOMARKERS OF THERAPEUTIC TARGETS FOR NEUROCOVID

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Background:
Cognitive deficits (CD) post-acute mild to moderate COVID-19 are frequent and poorly understood.

Methods:
128 COVID-19 patients (age=46±15; 42% women; 95% English speaking background) as part of the ADAPT study, a prospective cohort (St Vincent's Hospital Sydney, Australia) were enrolled 2-month post diagnosis. Disease severity was assessed with 18 acute symptoms, lung function, and hospitalization status (39% mild, 51% moderate, 10% severe/hospitalised at risk of hypoxia; 34% treated comorbidities). Blood samples were taken 2-, 4-, 8- and 12-months. Cognition, and olfaction were assessed at 2-, 4- and 12-months. Lung functions, Interferon (IFN)-β and IFNλ1, anxiety and depressive symptoms were assessed at 2 months and pre-existing psychiatric conditions were recorded. Seven KP metabolites were measured by gas chromatography coupled with mass spectrometry and ultrahigh-pressure liquid chromatography. Raw neurocognitive data were corrected for demographics and practice effect. Standard and Linear mixed effect regression models with time effect (months post diagnosis) tested how the tested effects were associated and contributed to neurocognition changes (main and time interaction, and polynomials as appropriate).

Results:
Between, 16-26% had mild to moderate CD across the study period, and between 20-28% had anosmia; Disease severity was associated with anosmia at 2-month ($p=.05$), but not cognition. CD were more common in those with anosmia ($p=.05$), those with elevated quinolinic acid and kynurenine/tryptophan ratio ($p<.05$). Quinolinic acid ($p=.001$), 3-hydroxyanthranilic acid ($p<.0001$) increased over the study period. Cognition declined (-0.43 of a z-score [95% CI=-0.39 to -0.47], $p<.001$).

IFN-β was associated with elevated quinolinic acid and kynurenine. Of the blood analytes only quinolinic acid, 3-hydroxyanthranilic acid, and kynurenine associated with cognitive decline ($p<.001$). Disease and medical factors, anxio-depression and the 2-month cognitive impairment status were not associated with cognitive decline.

Conclusion:
The KP as a unique biomarker of post-acute COVID-19 CD offers a therapeutic target.

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