Long COVID and Serotonin levels

Post-acute sequelae of COVID-19 (PASC, “Long COVID”) pose a significant global health challenge.

The pathophysiology is unknown, and no effective treatments have been found to date that adequately treat the symptoms of Long COVID.

Several hypotheses have been formulated to explain the etiology of PASC, including viral persistence, chronic inflammation, hypercoagulability, and autonomic dysfunction.

A mechanism has been proposed that links all four hypotheses in a single pathway and provides actionable insights for therapeutic interventions. PASC are associated with serotonin reduction.

Viral infection and type I interferon-driven inflammation reduce serotonin through three mechanisms:

1. diminished intestinal absorption of the serotonin precursor tryptophan;
2. platelet hyperactivation, thrombocytopenia, which impacts serotonin storage;
3. and enhanced MAO-mediated serotonin turnover.

Peripheral serotonin reduction, in turn, impedes the activity of the vagus nerve and thereby impairs hippocampal responses and memory. These recent findings provide a possible explanation for neurocognitive symptoms associated with viral persistence in Long COVID, which may extend to other post-viral syndromes.