



## Cognitive Consequences of COVID-19: The Missing Piece of Pandemic Crisis

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The global outbreak of COVID-19 in 2020, has affected the lives of all people. A proportion is due to recommendations to reduce the spread of the disease, which leads to isolation and negative neuroplasticity changes in the patients. On the other hand, cognitive disorders secondary to COVID-19 can develop in patients or exacerbate pre-existing cognitive disorders. Coronaviruses appear to be neurotrophic viruses that are found rapidly in the cerebrospinal fluid. Also, autopsy-based studies in patients with SARS found the virus in the hypothalamus and cortex in the brain (1, 2). After SARS-CoV and MERS-CoV infection, impaired memory, concentration, or attention were found during the acute phase and also after the illness (3).

Coronaviruses can cause many neurological disorders including; headache, olfactory dysfunction, movement disorders, encephalitis, and loss of consciousness, as well as respiratory disorders due to involvement of the brainstem and invasion of the cardiovascular center (4). Various studies have shown that activation of inflammatory cascade and cytokines play an influential role in the complications of COVID-19 disease, and there is a significant relationship between inflammatory pre-clinical responses such as CRP increase and cognitive impairment in patients (5).

An increase in inflammatory cytokines, including TNF- $\alpha$ , IL-1 $\alpha$ , IL-6, is associated with "disease behavior," which is somehow associated with decreased motivation, anxiety and depression, and impaired attention and concentration. Moreover, Anti-IL6 therapies can improve patients' condition and improve prognosis, and it seems that these treatments, like tocilizumab, can also improve patients' cognition. Disturbing factors such as social isolation, personal and family emotional trauma, and the presence of

anxiety and depression can also affect and exacerbate the patient's cognitive impairment.

Studies have shown that the hippocampus is vulnerable to the COVID-19 virus, which can lead to memory impairment in patients after recovery, as well as the possibility of long-term neurodegenerative diseases, which will require long-term follow-up studies. Studies have shown that CA1 and CA3 regions of the hippocampus are highly sensitive to the effects of coronavirus, which impairs memory, learning, and spatial awareness in patients (6, 7). Ritchie et al., demonstrated that individuals after the COVID-19 infection performed poorer significantly in reaction time, and this sustained attention disorder appeared to be associated with CRP and inflammatory factors (8)

### Conclusion

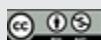
The effects of COVID-19 on cognitive impairment could be categorized into five groups:

- 1- Due to the direct effect of the virus on the central nervous system, Neurons, and Microglial cells: via direct mechanism through Blood-Brain Barrier transmission and also the indirect mechanism through the Olfactory nerve.
- 2- Due to the effect of other systems impairment on the cognitive status and cognitive sequences secondary to end-organ damage, for instance, liver and renal failure.
- 3- Inflammatory mechanisms secondary to cytokines storm, which could result in hippocampus atrophy.
- 4- Vascular mechanisms and elevated risk of stroke including; ischemic and hemorrhagic events.
- 5- Due to anxiety and depression secondary to social isolation on patients' cognition.

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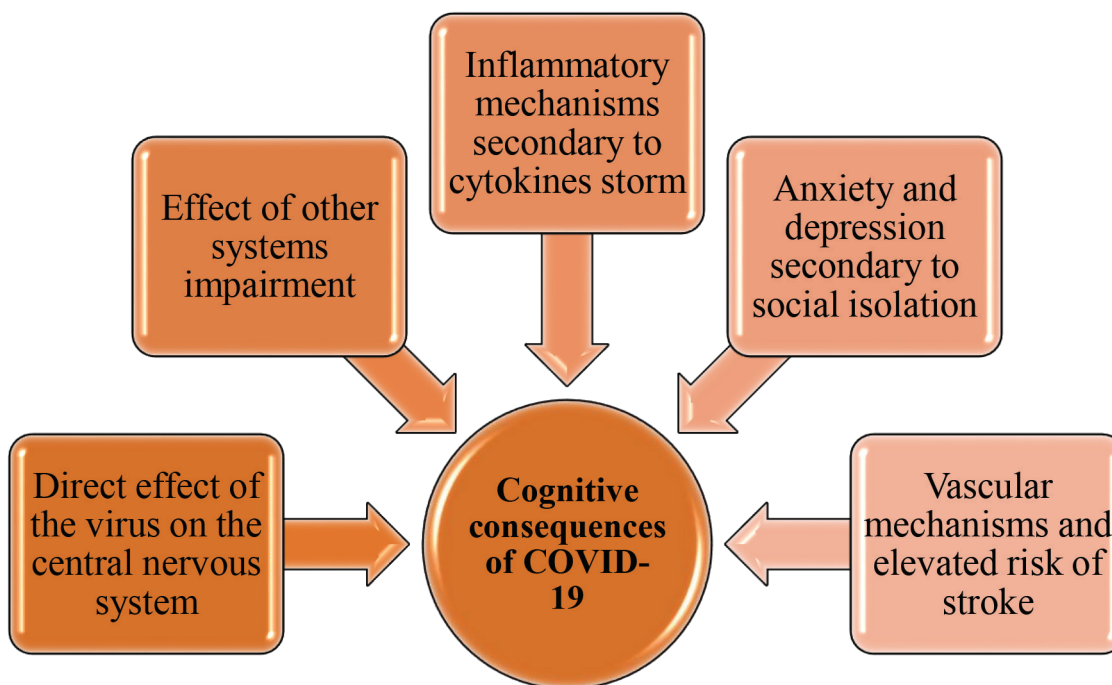
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Obviously, evaluation of these causes and determining their role in the patient's cognitive status has an effective role in the appropriate treatment and prevention of these cognitive disorders. Due to this issue, neuropsychological and cognitive evaluation of patients after recovery of the acute phase and in particular, patients with underlying cognitive impairment have a special place.

We proposed comprehensive neurocognitive assessment utilizing batteries including, Verbal-Auditory Learning Test (AVLT) (9), Montreal Cognitive Assessment (MOCA) (10), and Cambridge Computer Psychological Nerve Test Package (CANTAB). We should evaluate the patients' psychiatric symptoms which could probably influence cognitive function including, Beck Depression Inventory (11) and GAD-7 Anxiety Inventory (12).



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