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The Cognitive Impact of Coronavirus

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Coronavirus is a disease that leads to significant neuroinflammatory responses. There are many similarities in the way inflammation performs in several viral diseases. Specifically, the rise in pro-inflammatory cytokines occurs both in neurodegenerative diseases as well as coronavirus. These effects play a role in cognition that often results in the degeneration of cognitive processes. This degenerative process could lead to psychological illnesses such as depression and anxiety. The causal relationships and the intersection between psychological illnesses, cognition, and the neuroinflammatory response caused by coronavirus is relatively unknown, and so, a review of the current literature is conducted. This review concludes that there are many confounding variables - such as isolation and quarantine – which must be taken into account to better understand the interactions between the physiological (i.e., the neuroinflammatory response to coronavirus) and psychological factors that affect overall brain health.

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Introduction: Review of Literature

Cognitive impact of coronavirus

Coronavirus has a clear tie to neurological processes, but it is uncertain exactly what part of the brain it affects. There are many neurological effects of coronavirus: loss of smell and taste, syncope, acute cerebrovascular disease with varying strokes, and cerebral venous thrombosis [1]. Attention and memory deficits are presented with coronavirus infection as well. In mice following coronavirus infection, researchers observed a reduced size in the hippocampus which was related to attention and memory deficits [2]. Hypoxemia, especially a longer duration of it, was seen to be associated with cognitive impairment. Hypoxemia is a symptom of coronavirus [2]. Coronavirus has also been shown to cause neuronal death, especially within layers of the hippocampus. Cytokine release has been seen to be linked with coronavirus infection and follows usually after changes in memory, learning, and attention [2]. An excessive cytokine response has been implied with neuronal death in patients with coronavirus. The virus itself has been shown to trigger the progression of neurodegenerative and neuropsychiatric diseases of neuroinflammatory origin through its increased cytokine response [3].

Inflammation effects on cognition during Covid-19

Inflammation has been linked to cognitive decline in previous coronavirus studies [4]. Based on previous research, chronic neuroinflammation associated with high levels of cytokines and chemokines is related to the onset of some neurodegenerative diseases. Due to individuals having a lack of previous exposure to coronavirus, invasion of hematopoietic cells induces low expression of antiviral cytokines [3]. There is no secondary immune response available from memory. IFN-αβ and overexpression of pro-inflammatory cytokines and inflammatory chemokines are also presented as a response to coronavirus [3]. Those who are more severely affected by SARS-CoV show low levels of anti-inflammatory cytokines compared to those with a milder response [3]. Severe SARS-CoV-2 infection is associated with decreases in T lymphocytes but not B lymphocytes [3]. Previous cases have seen that coronavirus attacks the nervous system. One case had led to an acute necrotizing hemorrhagic encephalopathy, a disease that is related to intracranial cytokine storm and rupture of the blood-brain barrier [3]. Whether neuroinflammation is persistent or only on the onset of SARS-CoV-2 is unknown. With other inflammatory diseases such as Parkinson's and multiple sclerosis, there is an increase in the expression of pro-inflammatory cytokines. Similar inflammatory patterns within these diseases compared to SARS-CoV-2 have also led to increased gray matter damage.

Neuroinflammation also plays a role in the metabolism of neurotransmitters, causing changes to the HPA axis and affecting neuroplastic changes within the brain [3]. Pro-inflammatory cytokines are seen to be the basis for the disruption to these systems and an increase in these cytokines contributes to neurodegenerative pathology. SARS-CoV-2 can selectively bind to angiotensin-converting enzyme 2 (ACE-2), a receptor that is highly expressed in glial cells and neurons [3]. It's been previously seen that the virus causes neuronal death within mice through the ethmoid cribriform plate and invasion of the olfactory neuroepithelium [3]. In mice, it's also seen the virus could be detected within the CNS of a mouse up to a year later.

Cognition and Depression

Research has shown that poor cognitive function is associated with an increased risk of depression and social withdrawal [4]. ARDS is seen to be a symptom of coronavirus and those that have this symptom are also presented with alterations in mood such as depression and anxiety. A study conducted with coronavirus infected mice showed an association with altered mental status and personality change [2]. Findings have shown that depressive symptoms are associated with increases in proinflammatory cytokines [4]. Previous studies conducted have seen that those diagnosed with depression also had a decrease in overall cognitive abilities [4]. Those with depression perceived their environments and surroundings in a negative context, playing into the way they approach tasks and emotions [4].

Confounding variables: The impact of quarantine/isolation on depression

During a study conducted in China of the initial coronavirus outbreak in which the majority of respondents spent 20-24 hours of their day at home, 28.8% had moderate to severe anxiety symptoms and 16.5% had moderate to severe depressive symptoms [5]. Another study conducted with a population of University students saw a decrease in mental health during the covid-19 pandemic [6]. Although studies conducted do not show an association with the impact of quarantine/isolation on depression, a study conducted in 2016 of the elderly in social isolation can draw significant conclusions [7].

Social isolation has two uncorrelated constructs known as subjective and objective social isolation. Objective social isolation is the physical absence of seeing friends and family and participating in social events and smaller social circles due to external factors. Subjective isolation is the perspective and the perspective we build around isolation such as feelings of loneliness and a perceived shortage of a social network. In this study, it's seen that subjective isolation from friends and family resulted in higher levels of depressive symptoms [7]. Those who were isolated from

friends alone had increased depressive symptoms and a higher reporting of psychological distress. Objective social isolation is also related to greater depressive symptoms but not an increase in psychological distress [7]. But the differences due to objective social isolation were made insignificant once subjective social isolation was introduced.

Discussion

Very few research studies have been conducted looking at the neurological impact of coronavirus during the pandemic. This review aims to draw conclusions on the cognitive impact of coronavirus on individuals while also potentially identifying significant confounding variables. Due to the coronavirus pandemic, it's unclear whether depression is caused by people being infected with coronavirus or due to social isolation. Previous studies show that cognition is severely impacted by the inflammation of the nervous system. What's seen in viral diseases and with the coronavirus is an increased cytokine response especially in pro-inflammatory cytokines. This response is correlated with not only decreases in cognition but also an increase in depressive symptoms. The increased cytokine response has been seen to cause neuronal death as well. The heavily under-researched part is the interaction between depression, social isolation, and the decrease in cognition. Previous studies show that coronavirus leads to inflammation of the brain and increases the cytokine response. Many inflammatory diseases have been shown to have a direct impact on cognition. The increased cytokine response has been seen to correlate with the onset of neurodegenerative diseases. Cognition has been seen to decrease in those diagnosed with depression. From this, it's possible to say coronavirus has an increased risk of depression. It's also possible for depression to affect cognition and that cognition decreases due to depression. Out of a local population survey conducted of eighty responses, 16.3% tested positive for coronavirus, and of that 16.3%, 84.6% experienced a low mood or depression. Out of those who answered the survey with testing negative for coronavirus or unsure due to possible exposure, 67.2% stated they had a low mood or depression. This shows the interaction among depression, social isolation, and coronavirus.

Social isolation, a possible confounding variable, plays a large role in depression. Although there have not been direct studies conducted to show the impact of quarantine on psychological state, previous studies have shown that social isolation due to external circumstances results in increased depressive symptoms.

Further studies conducted could show the interplay between cognition and depression and whether specifically one causes the other. A limitation in this review is the lack of literature on coronavirus's cognitive effects due to its recent upbringing. Due to a lack of literature, it's difficult to draw appropriate conclusions on whether the pandemic itself or social isolation is what causes a rise in depressive cases. The literature shows inflammation plays a role in decreased cognition and that coronavirus has a significant impact on inflammation within the nervous system. The literature also shows that both being diagnosed with coronavirus and being socially isolated lead to an increased risk of depression. There have not been enough studies conducted to draw conclusions about the association between cognition and coronavirus and whether confounding variables, depression, social isolation, and news of the pandemic, play a role in this.

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