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Poster: SARS-CoV-2 Neuroinvasion

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Introduction

- Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), responsible for causing coronavirus disease 2019 (COVID-19), has been reported to cause various neurological manifestations and long-term sequelae in individuals following acute infection.
- Many infectious disease outbreaks throughout history have resulted neurological manifestations and post-infectious sequelae, indicating the importance of the infected individual's immune response to the virus of concern.
- Human postmortem brain studies indicate that human coronavirus variants and SARS-CoV can infect neurons and glia, implying SARS-CoV-2 may have similar neurovirulence (Aghagoli et al., 2020), but to date, the exact neurovirulence of SARS-CoV-2 remains unknown.
- SARS-CoV-2 neuroinvasion is postulated to be a result of direct neurotropism and indirect viral invasion of the Central Nervous System (CNS) due to a break down in the Blood-Brain-Barrier (BBB) (Erikson et al., 2021).

Reason for Topic Choice

- Working as a bedside nurse on a stroke unit (neurology) at a comprehensive stroke center has provided numerous clinical examples of the direct and indirect effects of SARS-CoV-2 on the neurovascular system and is the reason for choosing this topic.

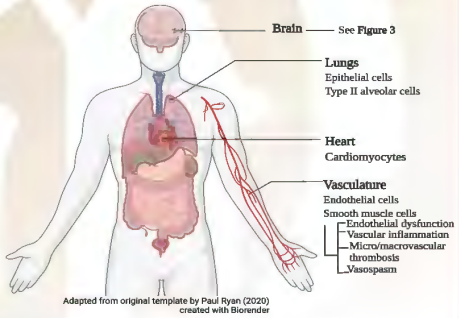
Signs & Symptoms

Isolated, sudden anosmia and ageusia, in the absence of nasal obstruction or rhinorrhea, suggests the relevance of early neurological involvement.

Other neurological clinical manifestations reported include:

- Seizure
- Altered mental status
- Acute ischemic stroke
- Ataxia & movement disorders
- Dizziness
- Headaches
- Demyelinating syndromes (such as Guillain-Barré)
- Various psychiatric/ behavioral manifestations
- long-term neurological

Figure 1
Host Tissues Known to Express Angiotensin Converting Enzyme 2 (ACE2)



Adapted from original template by Paul Ryan (2020) created with Biorender

Neuroinvasion, Neurotropic Pathways & Pathophysiological Processes

The expression and distribution of Angiotensin Converting Enzyme 2 (ACE2) suggest that SARS-CoV-2 may cause neurological symptoms through indirect and direct mechanisms (S. Al-Sarraj et al., 2021), as seen in **Figure 2** and **Figure 3** below (created using Biorender, with credit for original images cited).

Indirect

- The CNS is impacted by pathological inflammation and the cytokine storm that is triggered outside of the brain by COVID-19 (Burks et al., 2021).
- Disruption of the BBB provides a hematogenous route of entry for SARS-CoV-2 to invade the CNS.
- Studies have demonstrated an increase in cytokine serum levels as a result of SARS-CoV infection, consistent with the notion that cytokine overproduction and toxicity may be a relevant potential mechanism of neurologic injury, paralleling a known pathway of pulmonary injury (Aghagoli et al., 2021; see Figure 2).

Direct

- Multiple non-neuronal cell types present in the olfactory epithelium express two host receptors, ACE2 and TMPRSS2 proteases, that facilitate SARS-CoV-2 binding, replication, and accumulation (Butowt & Bilinska, 2020).
- The olfactory nerve and bulb serve as a conduit for CNS infection (Meinhardt et al., 2021) via neuronal and non-neuronal cells.
- *Neurotropism:* SARS-CoV-2 binds to the angiotensin-converting enzyme 2 (ACE2) receptor, expressed by neurons and glial cells (including astrocytes & microglia; see Figure 3A)
- Microglial reactivity, if initiated effectively, could orchestrate the clearance of SARS-CoV-2 in the CNS or trigger neuroinflammation (see Figure 3B) and contribute to the severity of the sequelae associated with SARS- CoV-2 neurotropism (Awogbindin et al., 2021).

Figure 2- Cytokine Storm, Inflammation & Damaged Lung Cells

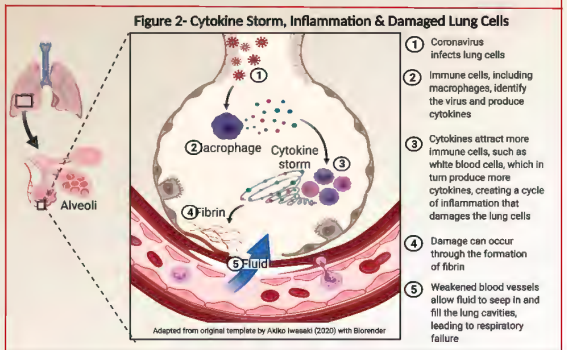
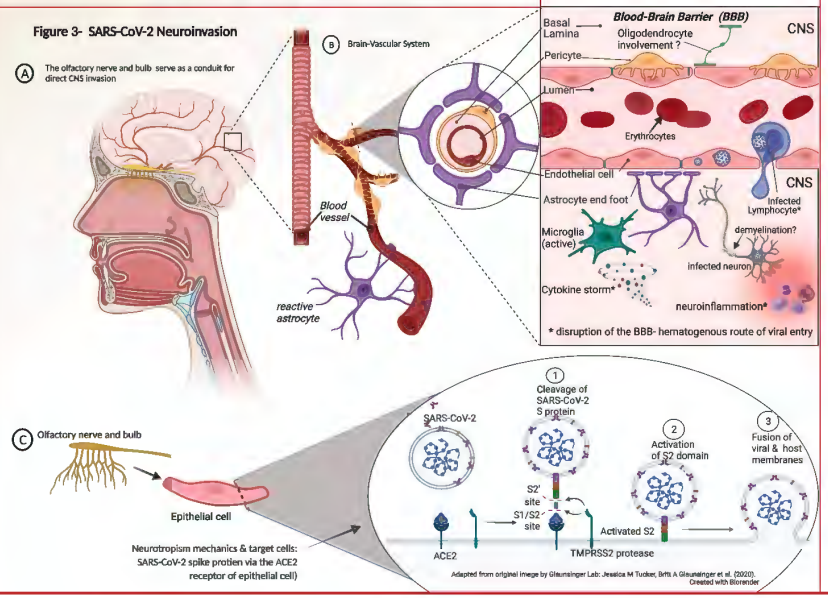


Figure 3- SARS-CoV-2 Neuroinvasion



Significance of Pathophysiology

- There is ample evidence in literature (postmortem human brain studies) suggesting endemic human coronaviruses infect neurons and glia (Cevik et al., 2020), but to date, the neurovirulence of SARS-CoV-2 remains unknown.
- Post-mortem magnetic resonance imaging (MRI) analysis in COVID-19 patients demonstrated an asymmetry in olfactory bulb and aberrant brain parenchyma in 21% of samples thus further corroborating the relevance of trans-nasal CNS infection (Coolen et al., 2020).
- Direct neuron infection has potential to cause future neurodegenerative diseases in previously infected individuals (Awogbindin et al., 2021).
- Further studies should investigate the neurovirulence of SARS-CoV-2 and the future implications of various neurologic manifestations.

Implications for Nursing Care

Vaccine Hesitancy & Misinformation

- Data proves the efficacy and safety of COVID-19 mRNA vaccines for individuals 12-years and older in the United States (US), yet many are hesitant to get vaccinated, with 67% of unvaccinated adults believing at least one piece of misinformation regarding COVID-19 vaccination (Altman, 2021).
- The unprecedented amount of misinformation circulating on social media and cable news networks indicates a bigger health literacy problem in the US.
- Encourage vaccination in individuals 12-years and up in professional and personal life.
- See the U.S. Surgeon General's advisory on building a healthy information environment, *Confronting Health Misinformation:*

Long-term Follow-up & Monitoring

- One in twenty people who recover will experience *long COVID.*
- All healthcare providers that are in patient-facing roles and clinical practice should be aware of SARS-CoV-2 neurotropism and long-term neurologic sequelae.
- Based upon the available evidence to date, it is crucial for healthcare providers establish the underlying mechanisms of action related to the specific neurological manifestations that individuals exhibit in order to prevent neurological deterioration.
- Older adults are at higher risk of demonstrating neurological manifestations due to the processes involved in the pathophysiological processes involved with the human brain as it ages.

Telemedicine Considerations

- Best practices/standardization is urgently needed across specialties and primary care.
- Telestroke as a model
- Health equity and access should be considered with telemedicine.

Conclusions

- COVID-19 disease includes neurologic manifestations and long-term sequelae in some individuals.
- SARS-CoV-2 seems to be a vasculotropic and neurotropic virus.
- The evidence of a causal relationship between the SARS-CoV-2 virus and autopsy brain studies remains equivocal (S. Al-Sarraj et al., 2021).
- Further large-scale molecular/cellular investigations are needed to clarify neuropathological correlates with clinical features since SARS-CoV-2 neurovirulence remains unclear.
- Awareness is needed among those managing SARS-CoV-2-infected patients with CNS symptoms.
- COVID-19 vaccination of more individuals is needed in the US and globally; misinformation as a major barrier in the US.

References

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