

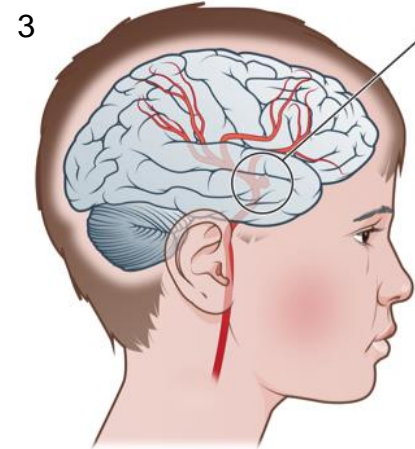
Association of SARS-CoV-2 Infection with Neurological Symptoms and Neuroimaging Manifestations in the Pediatric Population: A Systematic Review



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Background

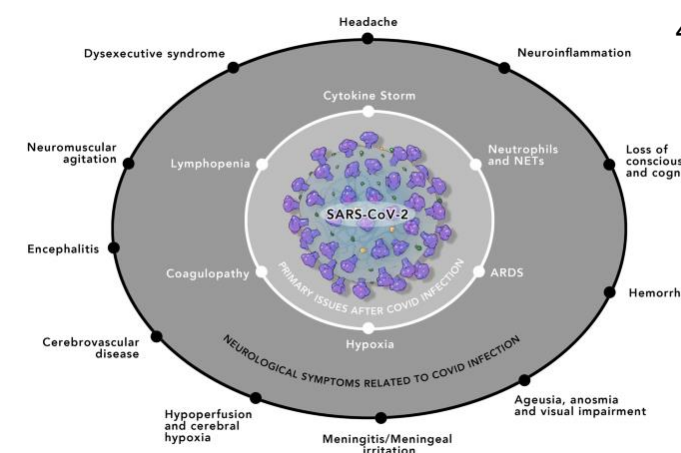


- Importance:** Neurological impairments have been widely reported in adults with COVID-19.¹
- Clinical Significance:** With increasing reports of multisystem inflammatory syndrome in children, it is important to characterize their associated neurological profile.²

Research Question

SARS-CoV-2 virus is known to have neurotropic abilities, using the **ACE2 receptor** as an entry way into host cells.²

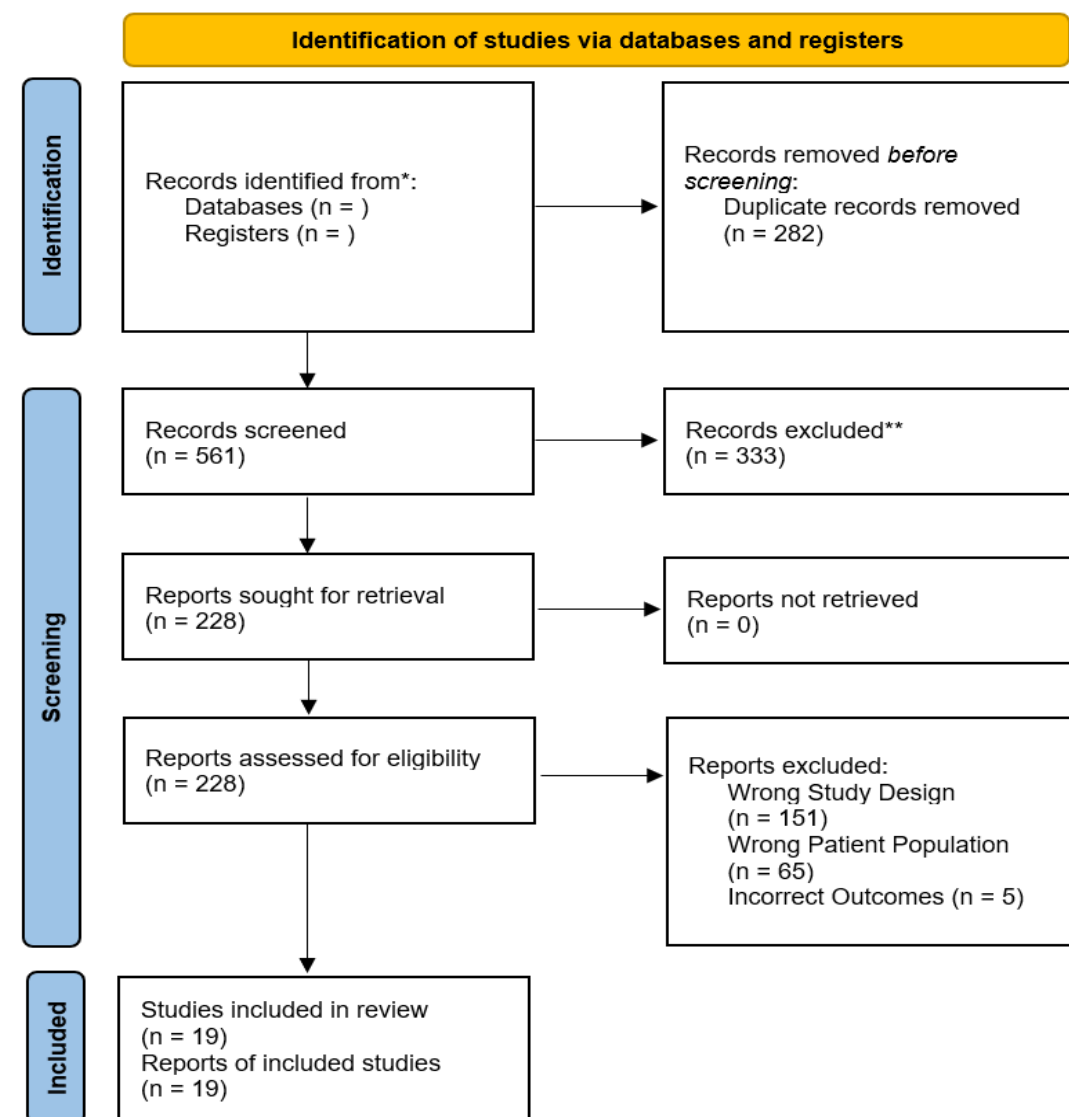
Goal: To determine the neurological symptoms & neuroimaging manifestations associated with SARS-CoV-2 infection in the pediatric population.



Key Findings

- 77% of patients with neurological abnormalities had **MIS-C**, (the most prevalent manifestation), followed by encephalopathy (20.9%) and neuroinflammation (20.6%).
- Drowsiness and muscle weakness were more common among **children** than adolescents, and agitation/irritability was more common among **children** than infants.
- MIS-C may manifest as part of a post-infectious immune response – similar to the mechanism involved in the COVID-19 related autoimmune meningoencephalitis observed in adults.

Search Strategy & Methodology



Eligibility Criteria:

- Individuals < 18 years with a **confirmed** first SARS-CoV-2 infection scanned for **structural & functional abnormalities** using brain CT, MRI, PET scan, or other modalities.
- All studies from **October 2019 to present** examining the impact of SARS-CoV-2 infection on **pediatric** brain structure & function.
- Excluded if **unconfirmed** cases of COVID-19, patients **with pre-existing comorbidities**, studies on animals, and studies **lacking explicit reporting** of neurological findings.

Age Stratification:

- Infants** = 0-1 years old
- Children** = 1-11 years old
- Adolescents** = 12-18 years old

Results

Sample Size:

Of the total **n = 6950** participants, **335** were identified with neurological symptoms or abnormal neuroimaging findings.

Neurologic Abnormalities:

- MIS-C** (n=258, 77.0%)
- Encephalopathy (n=70, 20.9%)
- Neuroinflammation (n=69, 20.6%)
- Gullian-Barre Syndrome (n=16, 4.8%)
- MERS (n=10, 3.0%)
- Infarct (n=9, 2.7%)
- Cerebral edema (n=5, 1.5%)
- Vasculitis (n=2, 0.6%)

Neurologic Symptoms:

- Seizure** (n=57, 17.0%)
- Headaches (n=42, 12.5%)
- Stroke (n=22, 6.6%)
- Fatigue/lethargy (n=13, 3.9%)
- Muscle weakness (n=32, 3.9%)
- Agitation (n=12, 3.6%)
- Drowsiness (n=11, 3.3%)
- Hallucinations (n=11, 3.3%)
- Gait instability (n=10, 3.0%)
- Cerebellar ataxia (n=5, 1.5%)
- Dysarthria (n=3, 0.9%)

Imaging Modalities:

- MRI** (n= 141 of 211)
- CT (n= 65 of 211)
- PET (n= 7 of 211)
- CT/MRI (n= 5 of 211)

Neurological Impairments on Imaging:

- Lesions of the corpus callosum** (n=32, 9.6%)
- PNS involvement (n=31, 9.3%)
- CNS involvement (n=20, 6.0%)
- Brainstem (n=15, 4.5%)
- Cerebrum (n=1, 0.3%)
- Cerebellum (n=12, 3.6%)
- Frontal lobe (n=6, 1.8%)
- Frontal-parietal cortical (n=1, 0.3%)
- Hippocampus (n=2, 0.6%)
- Midbrain (n=1, 0.3%)
- Temporal lobe (n=6, 1.8%)
- Parieto-occipital cortical (n=2, 0.6%)
- Occipital lobe (n=1, 0.3%)
- Olfactory gyrus (n=1, 0.3%)

Figure 1. Flow Diagram for systemic review based on PRISMA criteria. From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al.

Future Considerations

- Determining which subsets of the pediatric population are more susceptible to the aforementioned autoimmune conditions (in order to target therapies).
- Consider the impacts of vaccination status in the prevention of the discussed neurological abnormalities.

Acknowledgements

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