Neurological Implications of COVID-19 Infections

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Neurological manifestations in COVID-19

- 36.4% of 214 patients
- Symptoms: dizziness, headache, and impaired consciousness
- Severe infections represent disturbance in neurological function
- No definitive reports of SARS-CoV-2 detection in CSF.
  - CSF positive for SARS-CoV-2 but no clinical or laboratory details were provided, and PCR techniques are at risk of sample contamination
  - SARS-CoV-2 entry: ACE2 and TMPRSS2
    - minimal expression in brain tissue
    - Oligodendrocyte express both genes => risk of white-matter disease
    - para-infectious neurological diseases: Guillain–Barré syndrome, transverse myelitis, or acute disseminated encephalomyelitis

Clinical Characteristics of Patients With COVID-19 in CNS

Characteristic	No. (%)			*P* value[a]
	Total (N = 214)	Severe (n = 88)	Nonsevere (n = 126)	
CNS				
Dizziness	1 (1-30)	1 (1-30)	1 (1-14)	NA
Headache	1 (1-14)	1 (1-3)	3 (1-14)	NA
Impaired consciousness	8 (1-25)	10 (1-25)	1 (1-3)	NA
Acute cerebrovascular disease	9 (1-18)	10 (1-18)	1 (1)	NA
Ataxia	2 (2)	2 (2)	NA	NA
Seizure	2 (2)	2 (2)	NA	NA
PNS				
Impairment				
Taste	2 (1-5)	3 (1-3)	2 (1-5)	NA
Smell	2 (1-5)	1 (1-4)	2 (1-5)	NA
Vision	2 (1-3)	3 (2-3)	1 (1)	NA
Nerve pain	1 (1-1)	1 (1-1)	1 (1)	NA
Skeletal muscle injury	1 (1-11)	1 (1-11)	1 (1-6)	NA

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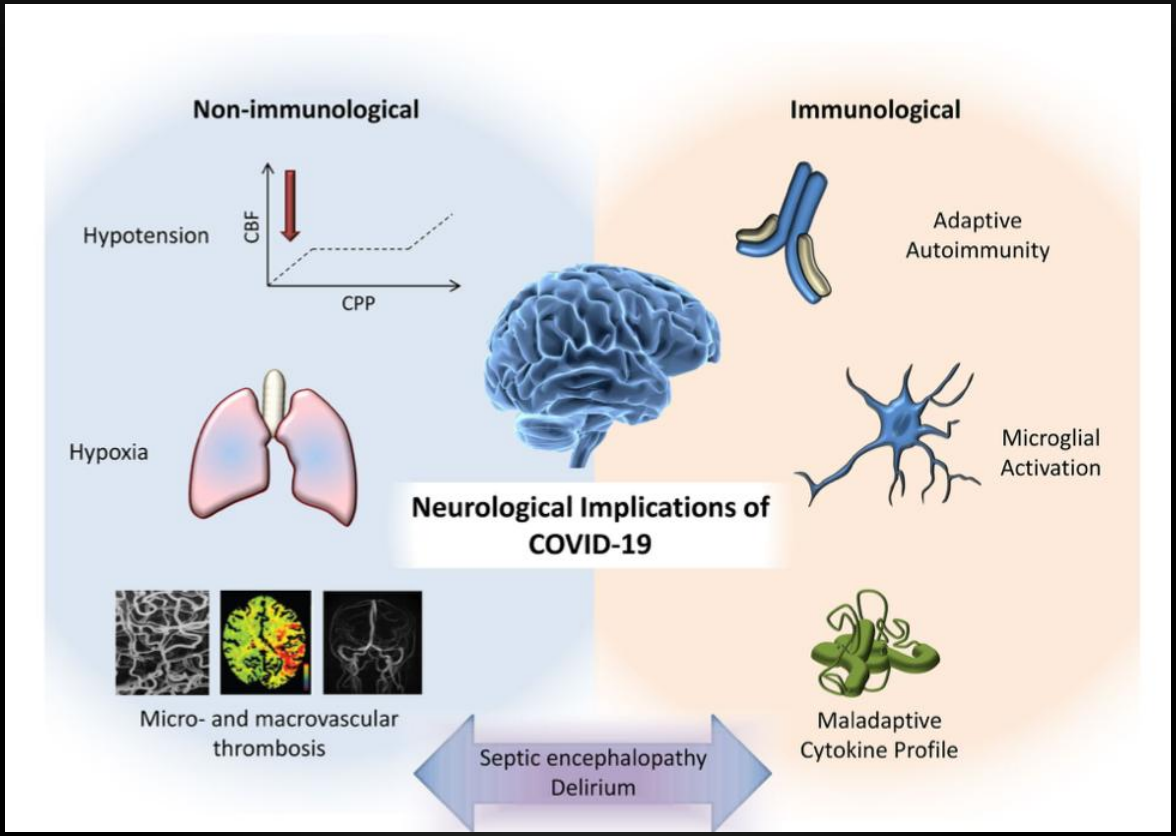
Putative mechanisms underlying neurological consequences of COVID-19



Patients with neurological conditions requiring treatments

- Immunosuppressant medication, corticosteroids
  - Risk of worsen outcome
  - some benefit in the most severe cases of COVID-19-related ARDS
  - Routine corticosteroids use is currently avoided
- Intravenous immunoglobulins (IVIg) or plasma exchange (PLEX)
  - May even be of potential benefit
  - IVIg is associated with an increased risk of thromboembolism
- Cyclophosphamide or rituximab
  - highest risk treatments

Suggested

Potential chronic neurological consequences

- Increased burden of long-term cognitive impairment ???

Table 1 Tiered approach to facilitate parallel development and rapid deployment of investigations of neurologic manifestations of COVID-19. Centers can elect to participate in Tier 1, Tiers 1 + 2 or 1 + 3, or Tiers 1 + 2 + 3

	Design considerations	Common data elements	Ethical board considerations	Participating centers	Implementation considerations
Tier 1	Prospective Registry Simple inclusion and exclusion criteria Small # of core data elements => Low burden to research team Low data granularity, capture basic groups Outcomes: acute phase outcome, e.g., mortality	Core	Qualifies for expedited review Qualifies for waiver of consent	All centers All centers able to participate regardless of resource levels Many centers Large sample size	Practical in COVID-19 pandemic and compatible with infection containment: No direct contact with study subjects All data can be collected remotely from electronic health records or via telecommunication with clinical team Highly pragmatic (lean) workflow
Tier 2	More detailed clinical and neurodiagnostic data collection. Examples: Detailed neuroexam Clinical laboratory data Clinical imaging/neurophysiologic data Outcome: global Functional outcome assessment beyond mortality. Acute + subacute phase outcomes	Basic	Likely require full board review Likely require informed consent	Able/willing centers participate Smaller # of sites compared to Tier 1 Smaller overall sample size but more granular outcome	May require contact with study subjects—possibly utilize telecommunication tools to reduce exposure risk More onerous and granular data collection Standardization considerations in clinical laboratory, imaging, and electrodiagnostic data Missing data considerations
Tier 3	Advanced, nonstandard neurodiagnostics (e.g., advanced MR imaging) Prospective biospecimens collection (CSF, blood, other) for experimental biomarkers investigation Possible postmortem tissue study Longitudinal study to capture subacute and long-term events	Supplemental	Requires full board review Requires written informed consent	Small # of centers with necessary resources participate Smaller # of sites Smaller overall sample size but with longitudinal data and biomarker data	Requires direct contact with subject or specimen, higher risk for exposure Biospecimens will need biocontainment facilities for banking/storage Advanced neurodiagnostics resources available at participating centers Standardization considerations in experimental biomarkers (molecular and imaging)


感謝聆聽