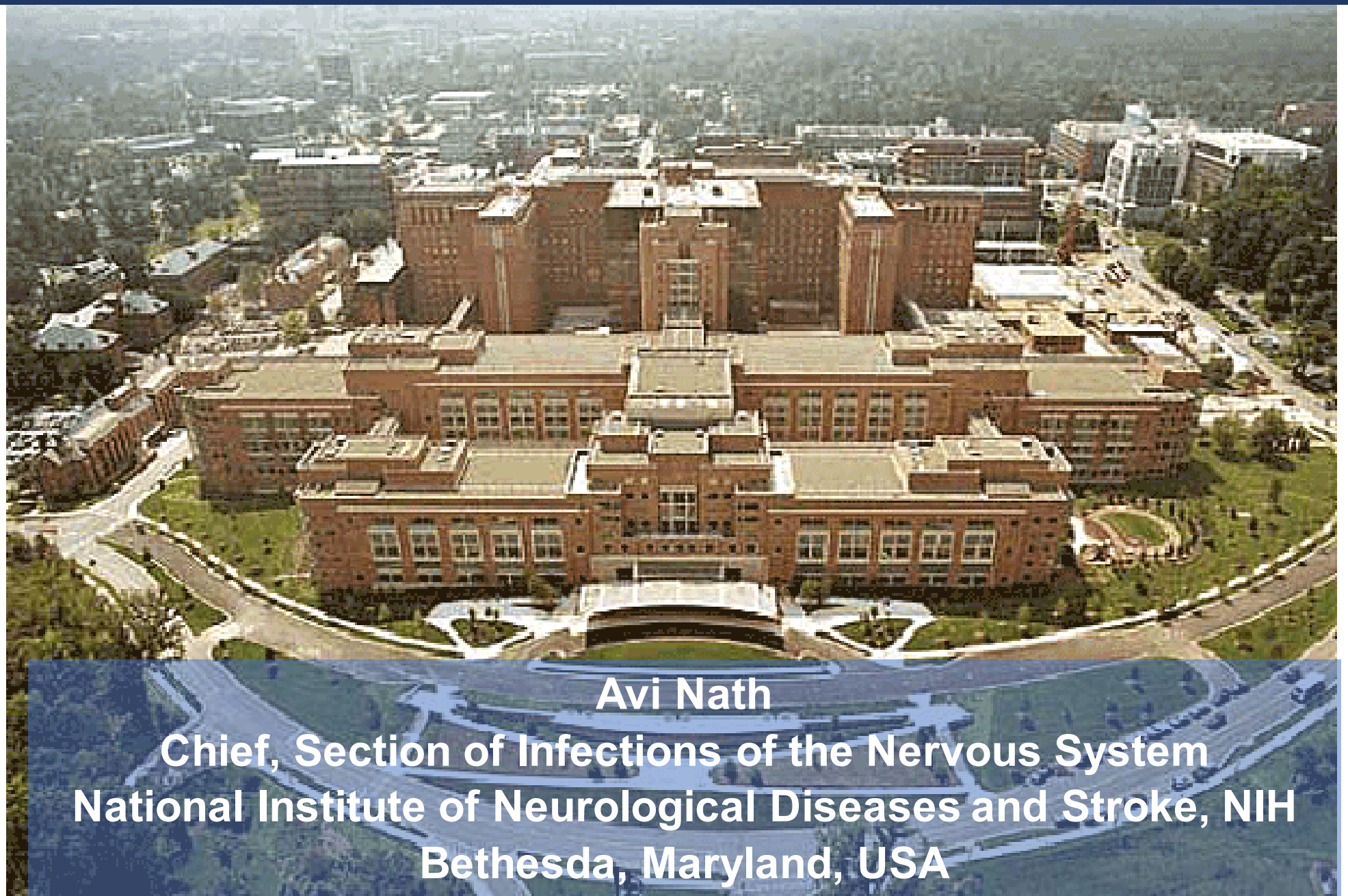
ME/CFS and Neuro-COVID-19

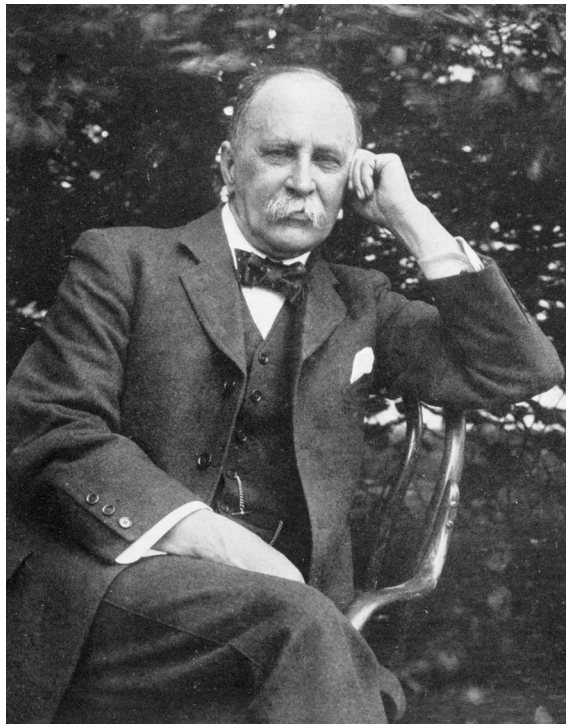


Avi Nath

Chief, Section of Infections of the Nervous System

National Institute of Neurological Diseases and Stroke, NIH

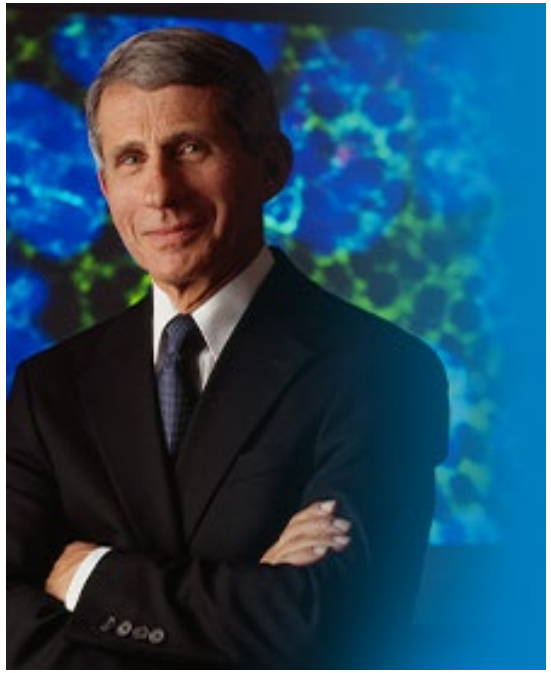
Bethesda, Maryland, USA



Humanity has but three great enemies: fever, famine, and war;

of these by far the greatest, by far the most terrible, is fever.”

Sir William Osler, 1896



“-----in a human-dominated world, in which man’s activities represent aggressive, damaging, and unbalanced interactions with nature, we will increasingly provoke new disease emergences. COVID-19 is among the most vivid wake-up calls in over a century.”

Anthony S. Fauci and **David M. Morens**

CORONAVIRUSES
All human coronaviruses cause neurological complications

Table 1. Human coronavirus *in vitro* properties.

Human Coronavirus	Genus	Genogroup	Receptor
HCoV-OC43	betacoronavirus	2A	O-acetylated Sialic Aicd (Protein Receptor Unknown)
HCoV-229E	alphacoronavirus	1B	APN
HCoV-HKU1	betacoronavirus	2A	O-acetylated Sialic Aicd (Protein Receptor Unknown)
HCoV-NL63	alphacoronavirus	1B	ACE2
SARS-CoV	betacoronavirus	2B	ACE2
MERS-CoV	betacoronavirus	2C	DPP4

Totura and Bavari 2019

Neurological Complications of COVID-19

Parainfectious manifestations

Anosmia
Myalgia/myositis

Encephalopathy
Stroke
Meningitis/encephalitis
Seizures
Ondine's curse(?)

Sensory neuropathy

Post-viral syndromes

Acute disseminated encephalomyelitis

Acute necrotizing hemorrhagic encephalopathy

Transverse Myelitis

Guillain Barre Syndrome

Acute Polyradiculoneuritis

Multisystem inflammatory Syndrome (Kawasaki's disease

Myalgic encephalomyelitis/chronic fatigue syndrome

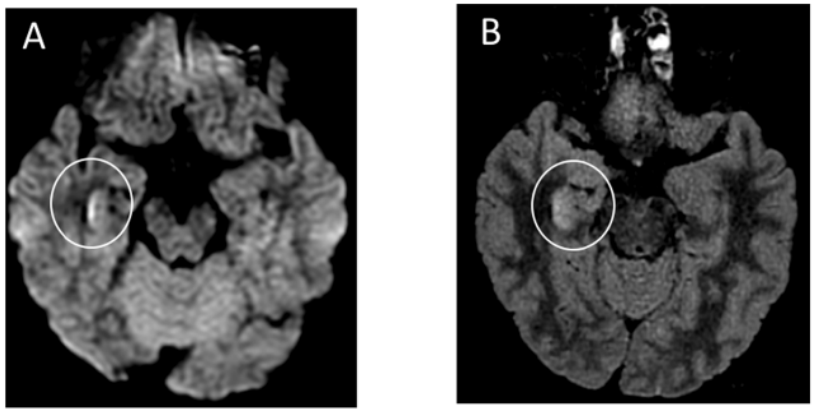
Dysautonomia

Toscano et al., NEJM 2020; Zhao et al. Lancet Neurol 2020; Zhang et al., MedRxiv 2020

Nath, Neurology 2020

Encephalitis

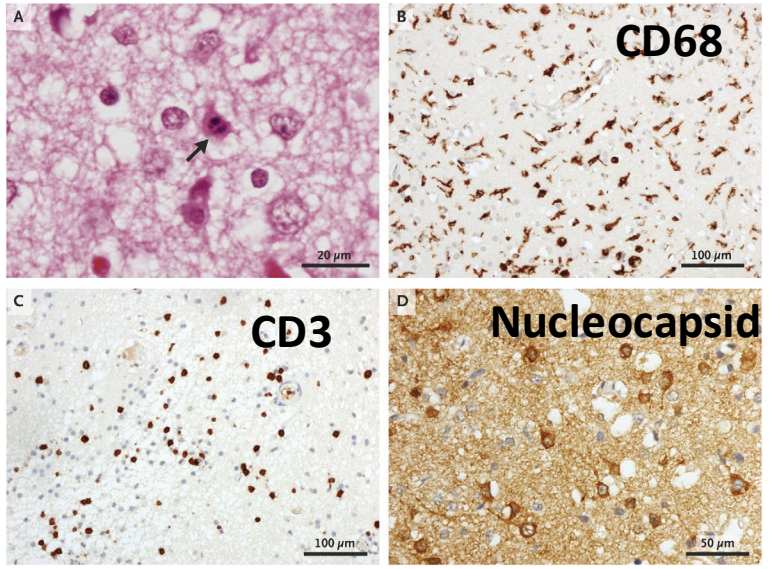
24 yr male
Fever
Loss of consciousness
Generalized seizure
Neck stiffness
Cerebrospinal Fluid: SARS-CoV2



SARS-CoV-2

Moriguchi et al., Int J Infec Dis 2020

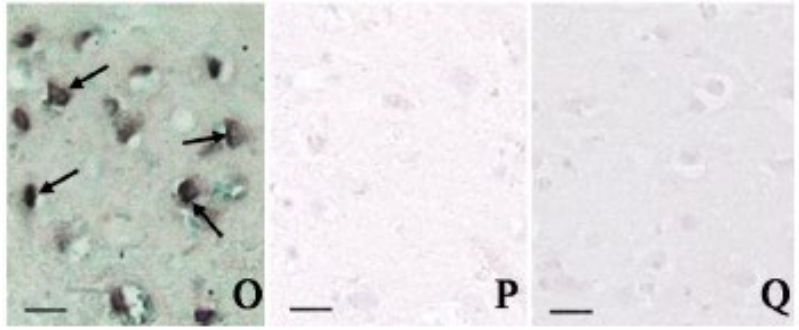
11-month male
Severe Combined Immunodeficiency



CoV-OC43

NEJM 2016

Viral RNA detected in 8 out of 8 patients in hippocampal neurons



SARS

Gu et al., J Expt Med 2005

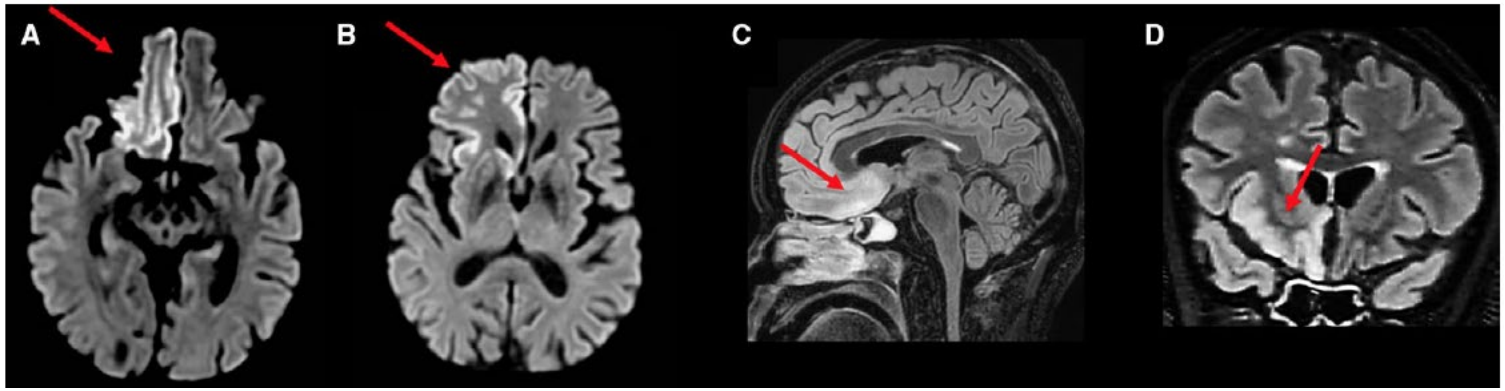
Encephalopathy with COVID-19

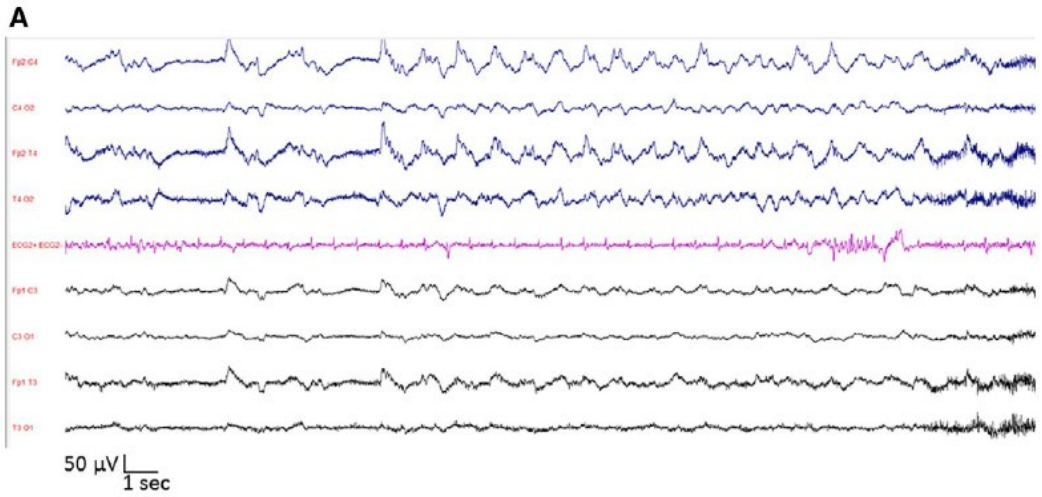
- 1/3 of hospitalized patients had altered mental status
- Hospital stay was 3 times as long
- 2/3 unable to manage activities of daily living upon discharge
- Independent of severity of respiratory disease
- Encephalopathy more common in older patients
- Neurological symptoms more common in young

Liotta et al., 2020

Pattern of frontal lobe involvement suggest viral transmission from olfactory pathways

Olfactory pathway

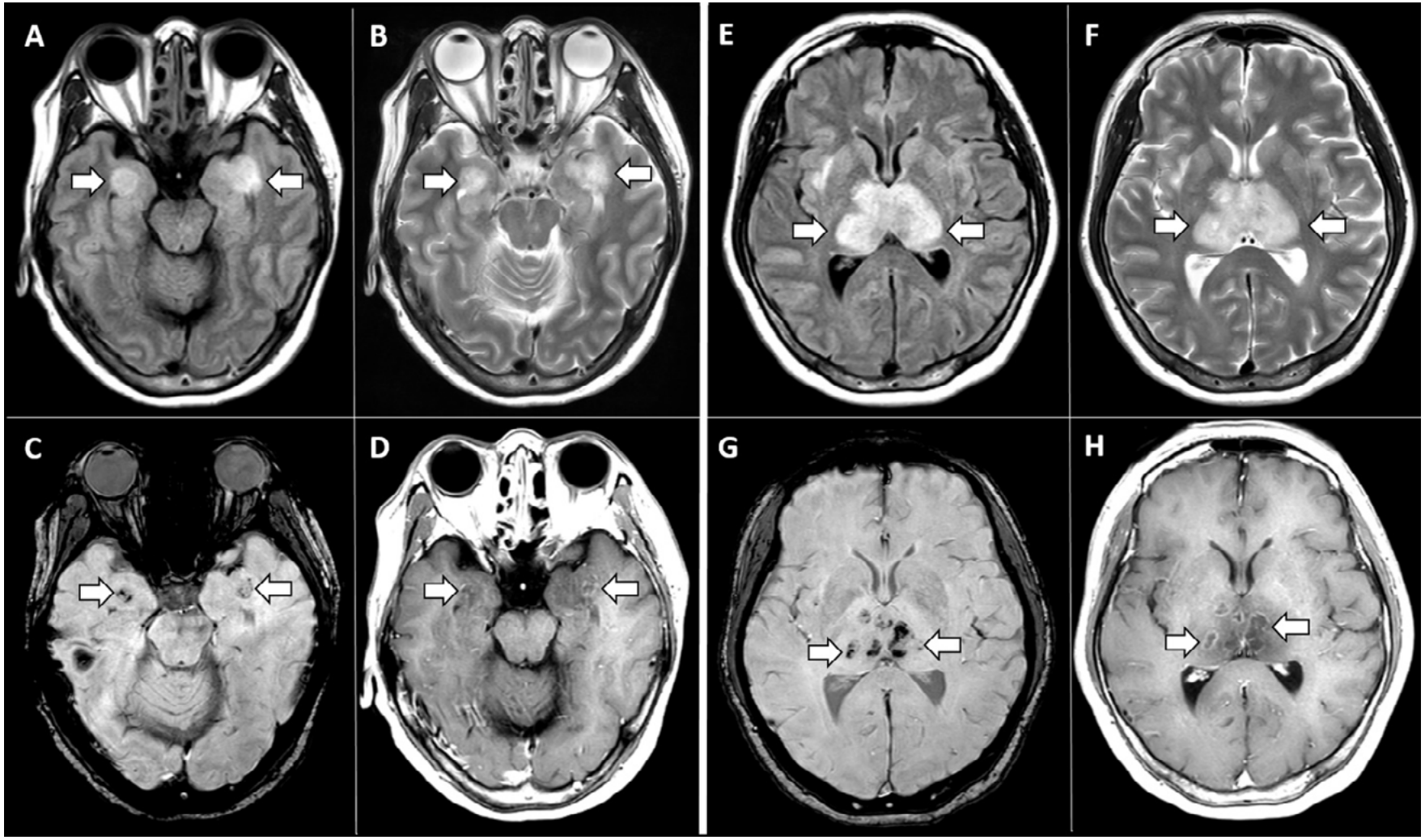




60 yr male
ICU for status epilepticus
Chest infection with SARS-CoV-2
CSF: normal virus PCR negative

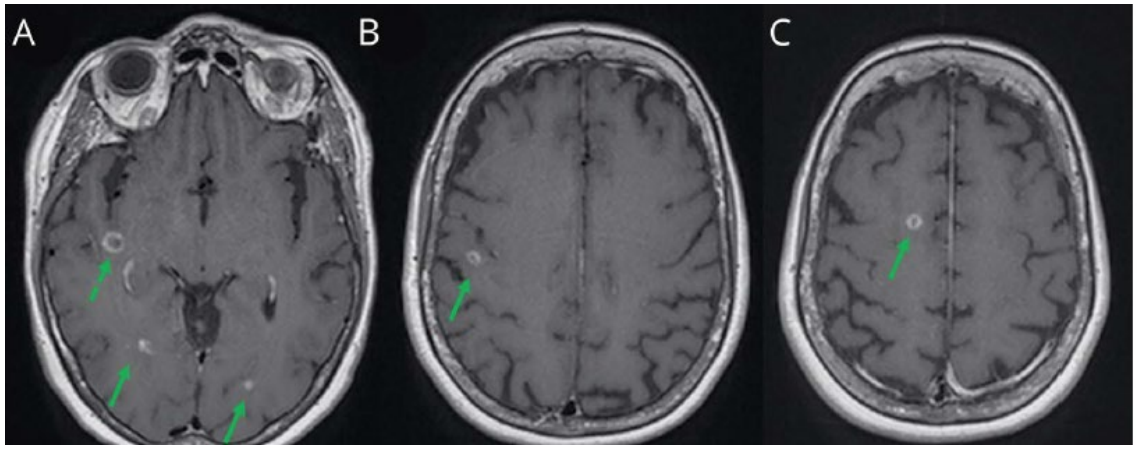
Acute Necrotizing Hemorrhagic Encephalitis (COVID-19)

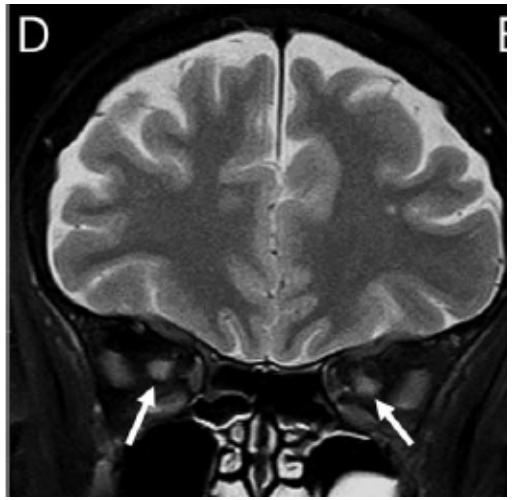
Female
Late 50's
Fever, cough altered mentation for 3 days
Acute respiratory distress syndrome
SARS-CoV2+



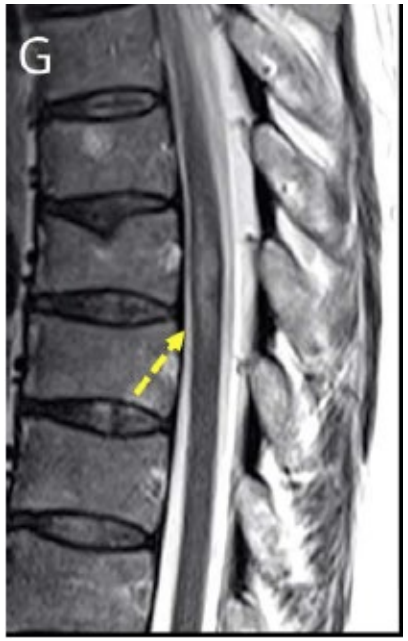
Poyiadji et al., Radiology 2020

Acute Dissemimated Encephalomyelitis with COVID-19





Bilat optic nerve enhancement



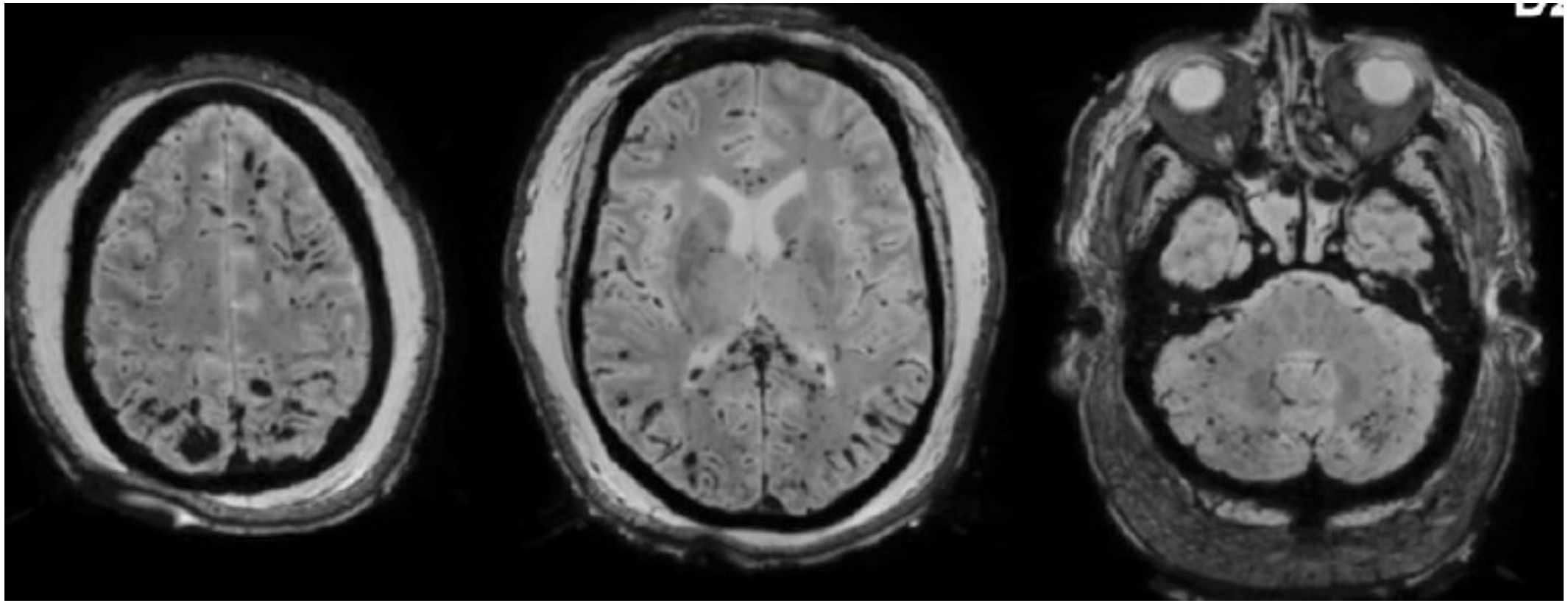
64 yrs, woman
CSF: 22 cells (CD3/CD4)
PCR positive in CSF
IgG for SARS-CoV-2 + in CSF
Treated: IVIG and High dose steroids

T8 lesion

AQ4 and MOG antibody negative

Novi et al., Neurol Neuroimmunol Neuroinflamm 2020

Microhemorrhages in brain (COVID-19)

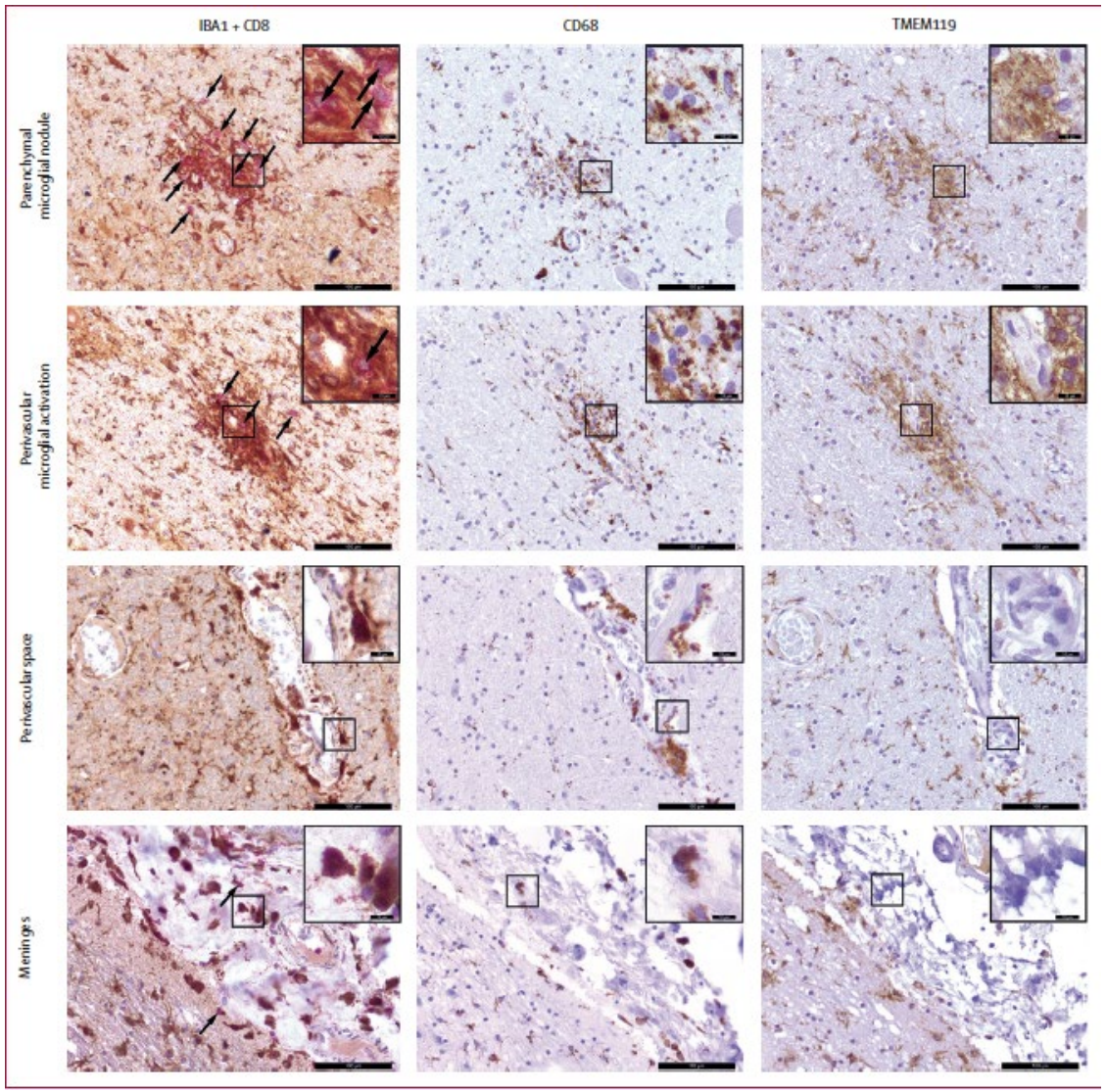


Coolen et al., MedRxiv May 8, 2020

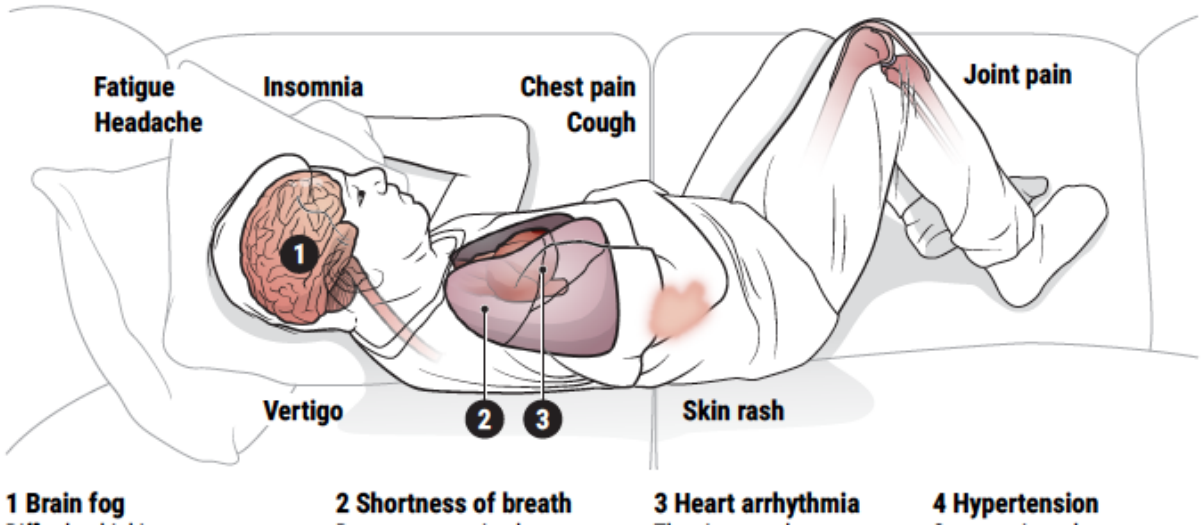
Neuropathology of patients with COVID-19 in Germany: a post-mortem case series

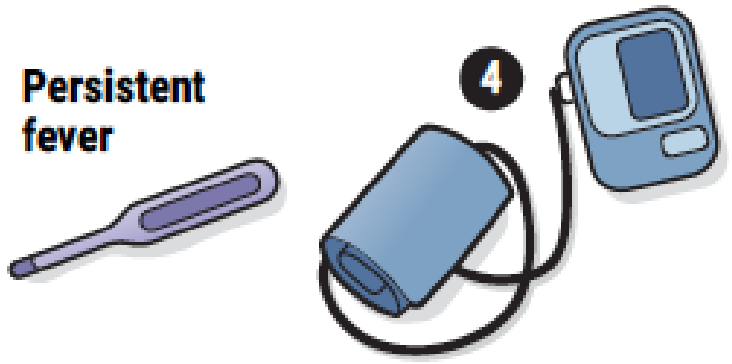
Jakob Matschke, Marc Lütgehetmann, Christian Hagel, Jan P Sperhake, Ann Sophie Schröder, Carolin Edler, Herbert Mushumba, Antonia Fitzek, Lena Allweiss, Maura Dandri, Matthias Dottermusch, Axel Heinemann, Susanne Pfefferle, Marius Schwabenland, Daniel Sumner Magruder, Stefan Bonn, Marco Prinz, Christian Gerloff, Klaus Püschel, Susanne Krasemann, Martin Aepfelbacher, Markus Glatzel

Lancet 2020



Long-Haul COVID





Overlap with Chronic Fatigue Syndrome

Science News 2020

Long-Haul COVID

Avindra Nath, MD

Neurology® 2020;95:559-560. doi:10.1212/WNL.0000000000010640

Table 1 Autonomic symptoms in Long-Haul COVID

1. Tachycardia upon mild exercise or standing
2. Night sweats
3. Temperature dysregulation
4. Gastroparesis
5. Constipation/loose stools
6. Peripheral vasoconstriction

Table 2 Possible etiopathogenesis of Long-Haul COVID

1. Unmasking of underlying comorbidities
2. Residual damage from acute infection
3. Persistent or restricted viral replication
4. Persistent immune activation
5. Unknown cause

Natural History of Post-Coronavirus Disease 19 Convalescence

- Protocol #: 000089
- Lead Associate Investigator: Brian Walitt

Phase A

- To observe and describe the range of medical syndromes that occur following an acute COVID-19 infection.

- Study population: 1000 adults who are within six months of their convalescence from an acute COVID-19 infection

- telephone interviews and internet-based questionnaires

SCHEMA FOR PHASE A

Participants contact the NIH for participation in the Post-COVID Convalescence Protocol.

1st Phone call:

Eligibility interview.
Documentation of positive COVID-19 testing will be collected.

2nd Phone call:

Verbal Informed Consent
Telephone survey
Log in for Internet based questionnaires

Participants may be

recontacted by study personnel,
referred to other NIH protocols, and may
continue to complete optional internet-based questionnaires for three years.

Phase B

- In person evaluation at NIH CC
- Focus on identifying patients who overlap with ME/CFS

Phase C

- In depth evaluation
- Focus on patients who overlap with ME/CFS

Phase D

- Longitudinal follow up

An Observational Study of Neurologic Function after COVID-19 Infection

Protocol #: 000094

Lead Associate Investigator: Bryan Smith

AIMS

- Primary Objective: To investigate structural abnormalities by brain MRI in those with prior SARS-CoV-2 infection and persistent neurologic symptoms.

- Secondary objective: To investigate other components of neurologic function in those with prior SARS-CoV-2 infection and persistent neurologic symptoms.

- MRI protocol optimized to detect COVID-19-associated disease.
- Neurological Assessment
- Autonomic Testing

- Study population: 50 participants
- Recruitment: Screening phase of Protocol 000089