Measuring cognitive and brain changes in COVID-19 survivors using neuropsychology and neuroimaging

University of Nebraska Medical Center, Department of Neurological Sciences

CONTRIBUTORS:

- Thomas A. DeCesare
- Lillian Behm
- Connor J. Phipps
- Marco A. Gonzales-Castellon
- Matthew White
- Maximiliano Hawkes
- Vaishali Phatak
- David E. Warren

Abstract

Measuring brain and cognitive variables in COVID-19 survivors is highly significant to public health because of the enormous number of recovered patients (many millions) and the high incidence of cognitive complaints among survivors (up to 50% report “brain fog”). In this project, we will recruit a group of COVID-19 survivors who were treated at UNMC and a comparison group of non-COVID-19 patients with similar symptoms for a study of cognitive deficits and brain structure/function. This will provide preliminary data describing cognitive and brain changes associated with COVID-19 as well as the relationship between cognitive, brain, and disease variables.

Introduction

The lasting health consequences of COVID-19 remain unknown — including for brain health and cognition. Early evidence suggests that:

1) SARS-CoV-2 can be found in brain tissue *post mortem*[6]
2) Significant pathology is often evident in the brains of COVID-19 patients[6]
3) Neuroimaging (including *in vivo*) can reveal pathology such as white matter abnormalities, ischemic infarcts, and cranial nerve changes[1,7,8,14]
4) Neurological findings are frequently observed in COVID-19 patients[2–5,9,18]
5) Subjective and objective cognitive changes have been observed in many COVID-19 survivors[10,11]

These neurological effects of COVID-19 highlight brain and cognitive challenges related to recovery from the disease. Further, recovery time is highly variable.

Methods

Inclusion/Recruitment

We will be enrolling COVID-19 survivors with no prior cognitive complaints who were treated at UNMC for moderately severe COVID-19 (hospitalization, supplemental O_2, NOT intubated/ventilated)

We will use the opt-in registry managed by UNMC’s Health Record Data Access Core to identify two cohorts:

1) Patients treated for COVID-19 at our institution who experienced moderately severe disease
2) Patients treated at our institution for non-COVID-19 respiratory complaints

Name	Type	Dur.	Description
localizer	T2	0:44	Localizers to set up scan geometry
fmap	SE	1:04	Spin echo field map for distortion correction
rs-fMRI	EPI	10:00	Resting-state fMRI, eyes-open fixation.
3D T1	T1	6:38	Whole-brain T1-weighted anatomical image
3D T2	T2	5:57	Whole-brain T2-weighted anatomical image
FLAIR	TI	5:02	Whole-brain FLAIR anatomical image
SWI	T2	6:37	Whole-brain susceptibility-weighted image
DTI	DWI	9:58	Whole-brain diffusion-weighted image
pCASL	ASL	5:29	Pseudo-continuous arterial spin labeling
Total		**56:47**	Approx. 1 hour with setup, instructions, exit

Expectations

We predict that cognitive and brain measures in COVID-19 survivors will differ from normative expectations for age, sex, etc., and further that cognitive and brain outcomes will be correlated with disease variables (time in hospital, time on supplemental O_2, symptom severity).

Measures to be Collected

Questionnaires:

- Questionnaire data assessing subjective cognitive complaints, subjective symptoms post-COVID-19, and factors related to mood

Cognitive Assessments:

Table 1. NIH Toolbox: constructs addressed, measures included, and time required.

Construct	Measure	Test Time
Attention & Exec. Functions	Flanker Inhibitory Control and Attention	3 min.
Episodic Memory	Picture Sequence Memory	7 min.
Working Memory	List Sorting Working Memory	7 min.
Language	Picture Vocabulary	4 min.
Language	Oral Reading Recognition	3 min.
Executive Function	Dimensional Change Card Sort	4 min.
Processing Speed	Pattern Comparison Processing Speed	3 min.
Total	**—**	**31 min.**

Brain Variables:

Manual:

- Derived from clinical over-read of brain data and assigned a score from 0-3
- Include WM abnormalities, ischemic infarcts, and involvement of cranial nerves

Automated:

- HCP’s automated processing pipeline will give us regional brain volume, cortical thickness, WM abnormalities, perfusion, and functional brain network status

Disease Variables:

- Information will be extracted from the participant’s EMR with her/his consent
- Variables include: duration of hospitalization, time on supplemental O_2, duration of fever >100.3ºF, degree of lung involvement on CT imaging, and development/duration of delirium

Conclusion

By assessing brain structure/function, cognitive abilities, and disease variables in a cohort of patients treated at UNMC, this study will make a novel contribution to the literature of COVID-19 by providing an unprecedented opportunity to test associations between brain, cognitive, and disease variables simultaneously.

University of Nebraska Omaha