



## Abstract

As the first wave of COVID-19 begins to pass, it is promising that many patients are indeed recovering. The most severe of these patients have undergone acute respiratory failure and have had hospital courses significant for prolonged intubation. It has been observed that these patients have presented with a variety of neuropsychological symptoms after extubation with these effects continued several weeks to months after initial infection. In this case study, five patients were selected based off criteria of >10 days spent intubated in the intensive care unit and >3 weeks spent in an acute care hospital after which they were transferred for rehab at least two weeks after having been initially diagnosed with COVID-19. These patients all exhibited similar neuropsychological symptoms which we postulate could be secondary to their initial infection with SARS-CoV-2.

## Introduction

The repercussions of COVID-19 are yet to be fully comprehended. It has been found that SARS-CoV-2 has produced multiple effects on multiple human body systems. It has been found that studies are lacking regarding the effects of the infection on the human central nervous system and related neuropsychiatric outcomes. Studies of past respiratory viral pandemics show that diverse neuropsychiatric symptoms can arise in the context of acute viral infection or after variable periods of time post infection. Reports from 18<sup>th</sup> and 19<sup>th</sup> centuries show that influenza pandemics have marked increased incidences of insomnia, anxiety, depression, mania, psychosis and delirium. During the 2009 influenza (H1N1) pandemic and other coronavirus infections (SARS-CoV-1 epidemic in 2003, and the Middle East respiratory syndrome coronavirus (MERS-CoV) outbreak in 2012), several neuropsychiatric sequelae were reported, including narcolepsy, seizures, encephalitis, encephalopathy, Guillain-Barre syndrome (GBS), and other neuromuscular and demyelinating processes. In order to determine which neuropsychiatric symptoms are most prominently affecting those diagnosed with SARS-CoV-2 infection, long term follow up will be required.

## Methods and Sample

Five patients were selected from a pool of patients who were admitted for acute rehabilitation status post COVID-19 infection at St Charles Hospital. Consistent to all of five of these patients was total of >10 days spent intubated in the intensive care unit and >3 weeks spent in an acute care hospital after which they were transferred for rehab at least two weeks after having been initially diagnosed with COVID-19. All patients reported acute symptoms of anosmia. All five patients reportedly developed one or more symptoms of delirium, metabolic encephalopathy, anxiety or PTSD during acute hospital course.

## Summary of Cases

### Patient # 1

63 year old male who presented to the hospital on 3/27 after which he decompensated requiring intubation from 3/28-4/28. Patient's hospital course was complicated by delirium and metabolic encephalopathy. Upon presentation to acute rehab, patient exhibited continued anxiety. Patient stated he had a history of chronic anxiety and was restarted on Lexapro. Patient had diffuse, generalized weakness.

### Patient # 2

42 year old female who presented to the hospital on 3/29 and was subsequently intubated for acute respiratory failure from 4/1-4/14. Psychiatry was subsequently consulted for anxiety and PTSD. Patient was started on Lexapro and Trazodone with reported good effects. Upon transfer to acute rehab, Lexapro was discontinued and patient was started on Xanax for anxiety/PTSD. Patient was also followed by neuropsychology throughout hospital stay with improvement in mood. Patient had diffuse, generalized weakness.

### Patient # 3

51 year old male who presented to the hospital on 3/27 requiring intubation from 3/31-4/21 with reintubation from 4/22-4/25. Patient noted to have hospital course significant for severe anxiety. Patient however refused treatment with medication. Patient presented with weakness greater in the upper extremities than lower extremities, with proximal weakness greater than distal weakness. Patient was evaluated by neurology with MRI brain unremarkable and MRI C-spine performed showing moderate bilateral neural foraminal stenosis at C4-5. Upon transfer to acute rehab, patient with continued anxiety but continued to refuse medication. Patient followed by neuropsychology.

### Patient # 4

50 year old female who presented to the hospital on 4/1 upon which she was intubated and underwent trach placement on 4/21 secondary to prolonged intubation. She was decannulated on 5/7. Upon presentation to acute rehab, patient was tachycardic with reported persistent palpitations and with no relief with high doses of Xanax. Patient stated she had history of anxiety. Psychiatry was consulted and medication adjustments were made. Patient presented with generalized, diffuse weakness.

### Patient # 5

53 year old male who presented to the hospital on 4/15 after which he was intubated on 4/17 until 4/26. Patient's hospital course was complicated by altered mental status and acute metabolic encephalopathy. Neurology was consulted and EEG was performed. EEG showed slowing without seizures. MRI was negative for ischemic lesions. Neurology hypothesized altered mental status could be secondary to prolonged infection, intubation, sedation or other CNS insult. Patient was started on 1:1 observation secondary to decreased cognitive function and safety awareness. Upon presentation to rehab, patient did not exhibit any signs of altered mental status or acute metabolic encephalopathy. However, 1:1 observation was continued secondary to lack of safety awareness and cognitive function. Patient presented with lower extremity weakness greater than upper extremity weakness, with greater weakness in the proximal muscles than distal.

## Discussion

Specific to COVID-19 include neuropsychological symptoms both in the acute phase of infection as well as post infection. Those acutely infected have reported encephalopathy or persistent alterations in consciousness. It is hypothesized that the encephalopathy could be secondary to the cytokine storm syndrome. A recent meta-analysis has shown evidence of persistent neurocognitive deficits up to 18 months post-discharge in intensive care patients. These patients acutely reported having dysfunction of olfaction and taste perception which may be among the earliest symptoms. For both olfactory and gustatory perception, SARS-CoV-2 infiltration of higher order structures within the CNS may be contributory to their dysfunction. Long-term neuropsychiatric complications of SARS-CoV-2 will require follow up over the next several months to years. However, these outbreaks have been associated with depression, anxiety and trauma related symptoms. Small case series have also described peripheral neuropathy and myopathy as well. It is however unclear if this is secondary to the infection itself, the immunologic response secondary to the disease or due to long term intensive care. Causality is yet to be confirmed.

## Conclusion

In conclusion, SARS-CoV-2, similar to other respiratory pandemics, has been shown to have many neuropsychological manifestations in patients who are acutely infected and subsequently recovering from infection. A causal relationship between these symptoms and the initial infection with the virus may not yet be established as secondary factors such as past psychiatric history, prolonged intubation or other CNS insults may also be contributing to the acute exacerbations of these neuropsychological sequelae. Further studies will be necessary and follow up of these patients will be necessary to determine how these patients will be affected long term.

## References

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