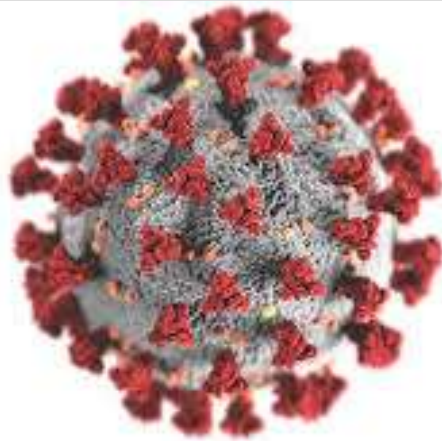


NEUROCOGNITIVE AND NEUROLOGICAL SEQUELAE OF LONG COVID: WHAT WE KNOW NOW

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REVIEW

COVID-19 is a respiratory and cardiovascular disease that is caused by the SARS-2 Coronavirus

The virus binds to ACE2 receptors, which are diffusely found throughout the body

Cells with these receptors die as the virus replicates

COVID-19 INFECTION

- The virus typically targets the lungs first, which results in an immune response
- When the immune system attacks the virus, it also kills surrounding cells
- This can result in lung damage and limits the supply of oxygen to the lungs
- Fluid will accumulate resulting in pneumonia
- In severe and critical cases, long-lasting lung damage may result from cytokine storms
- Even in milder cases, inflammatory reactions can result in post-viral complications

LONG COVID

- As of June 2022, approximately 40% of adults in the USA have had COVID
- An estimated 19% of survivors report at least one “long COVID” symptom
- This amounts to an estimated 13% of individuals in the USA have long COVID
- Symptoms include chronic fatigue, brain fog, respiratory issues, heart palpitations, headaches, dizziness, sleep problems, GI issues, myalgias, depression, anxiety

RISK FACTORS

- Age: Individuals between 50-59 are 3x at risk for long COVID compared to individuals who are over 80 years
- Gender: Almost 2:1 ratio of women over men
- Ethnicity: Ethnic minority populations
- Severity: Severe cases of COVID are more likely to result in disability
- Vaccination Status: Long COVID is more likely to occur in the unvaccinated (1:4 for double dose)
- Health Status: Obesity, COPD, respiratory illness, depression/anxiety

SEVERE COVID

- Patients hospitalized for ARDS may experience hypoxia
- Ventilators can result in permanent lung damage
- Severe COVID increases the risk of stroke and other neurovascular disease
- With the advent of vaccinations, the risk for severe COVID has decreased, but the rate of long COVID maintains

POST-VIRAL SYNDROME

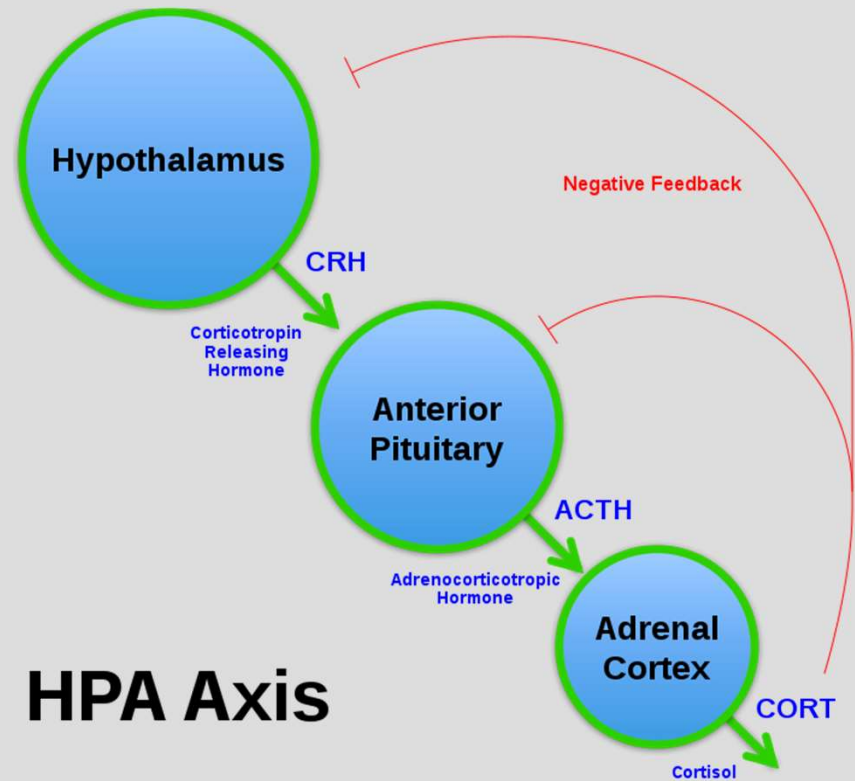
- PVS (and bacterial syndrome) is an established phenomenon in which patients experience residual symptoms for weeks, months, and years after an infection
- PVS is thought to be due to a change in which the brain and body react to infectious agents
- Persisting autonomic abnormalities may emerge that can result in dizziness, headaches, difficulty with temperature regulation, and anxiety
- Alterations of blood flow to the brain may trigger cognitive struggles in attention and concentration
- There may be a build-up of inflammatory cytokines in the CNS in response to a prior infection that responds adversely to subsequent infections

MYALGIC ENCEPHALOMYELITIS/CHRONIC FATIGUE SYNDROME

- ME/CFS can be triggered by herpes, mono, the flu, Lyme disease, HIV, rubella, and SARS I
- Long COVID may be another expression of ME/CFS and so literature on ME/CFS can provide insights on long COVID
- There is a likely autoimmune connection marked by chronic inflammation
- The hypothalamic-pituitary-adrenal (HPA) axis regulates stress through the cortisol hormone and is critical for immune response, digestion, energy use, and mood

HPA AXIS

Disruption in the HPA axis is linked to other conditions that involve some sort of intense trauma that might be physical or emotional including postconcussive syndrome and PTSD



DISRUPTED HPA AXIS

- When disrupted, the brain does not consistently monitor the needs of the body with regard to stress reaction
- Early trauma and stress in young animals can predispose them to have altered HPA functioning later in life
 - Similar model in humans?
- Chronic stress can result in neurological and physical symptoms that are akin to what is seen in postconcussive syndrome, PTSD, and postviral syndrome to various degrees!

AUTONOMIC DYSFUNCTION

ANS disturbance follows elevated stress response

Sympathetic nervous system: “fight or flight”

Parasympathetic nervous system: at rest

The ANS functions without conscious, voluntary control

A small subset of individuals develop persisting autonomic disturbance after illness (i.e., dysautonomia)

LINKING BACK TO LONG COVID...

- Long COVID may reflect a residual and lingering autoimmune disorder that a percentage of individuals are predisposed to develop after a broad, multisystemic infection
- Coupled with real-world stressors (pandemic or otherwise), the maintenance of such systems might be secondary to disruption in the autonomic nervous system (which may maintain the autoimmune disorder)
- Thus, the demarcation of “physiological” and “psychological” remains unclear and likely varies from individual to individual

POSSIBLE DIAGNOSTIC METHODS

- There is no single laboratory test that can diagnose long COVID, although some objective methods are available to detect symptoms associated with long COVID
 - Vestibular testing for balance, dizziness, ocular abnormalities
 - Blood-based biomarkers for vascular dysregulation
 - Neuroimaging (may only pick up residuals in severe cases)
 - Neuropsychological testing for cognitive and emotional symptoms

TREATMENT

- There is no cure for ME/CFA as of this time, and treatment is primarily symptomatic
 - Psychotherapy to address depression, anxiety, and stressors as they arrive
 - Medications to regulate blood pressure, dizziness, headaches, pain and mood
 - Sleep studies for apnea/other sleep disorders
 - Low-grade exercise to restore autonomic balance
- With long COVID/PVS, some individuals will have complete resolution of symptoms after an undefined period (months/years) but the possibility of permanent impairment must be considered

LONG COVID IN WORK COMP

THE FIRST CHALLENGE

- Long COVID is syndromic and based in part by patient's self-report
- No one diagnostic test can rule-in or out long COVID.
 - Rather, separate tests can assess for abnormal bloodwork, abnormal respiratory functioning, sleep issues, neurological symptoms, and cognitive symptoms
- Pain and mood are subjective indicators that depend on the patient's self-report
- Thus, the credibility of the patient (applicant) is important to establish in medical-legal cases

THE ROLE OF THE NEUROPSYCHOLOGIST

- No field is as equipped to tease out the role of subjective factors of brain dysfunction with objective signs of cognitive disability than the neuropsychologist
- Our tools can assess for credibility to a level that other practitioners cannot
- When credibility is established, an applicant's veracity in their self-report increases
 - Vital for establishing accurate levels of mood and subjective disability
- When not established, substantial medical evidence is not met for disability rating

RATING COGNITIVE DISABILITY

Table 13-6 Criteria for Rating Impairment Related to Mental Status

Class 1 1%-14% Impairment of the Whole Person	Class 2 15%-29% Impairment of the Whole Person	Class 3 30%-49% Impairment of the Whole Person	Class 4 50%-70% Impairment of the Whole Person
Paroxysmal disorder with preim- pairment exists, but is able to perform activities of daily living CDR = 0.5	Impairment requires direction of some activities of daily living CDR = 1.0	Impairment requires assistance and supervision for most activi- ties of daily living CDR = 2.0	Unable to care for self and be safe in any situation without supervision CDR = 3.0

RATING PSYCHIATRIC DISABILITY

The Global Assessment of Functioning (GAF)

Source: *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*

- **100-91:** Superior functioning in a wide range of activities, life's problems never seem to get out of hand, is sought out by others because of his or her many positive qualities. No symptoms.
- **90-81:** Absent minimal symptoms (e.g., mild anxiety before an exam), good functioning in all areas, interested and involved in a wide range of activities, socially effective, generally satisfied with life, no more than everyday problems or concerns (e.g., an occasional argument with family members).
- **80-71:** If symptoms are present, they are transient and expectable reactions to psychosocial stressors (e.g., difficulty concentrating after family argument), no more than slight impairment in social, occupational, or school functioning (e.g., temporarily falling behind in school work).
- **70-61:** Some mild symptoms (e.g., depressed mood and mild insomnia) OR some difficulty in social, occupational, or school functioning (e.g., occasional truancy, or theft within the household), but generally functioning pretty well, has some meaningful interpersonal relationships.
- **60-51:** Moderate symptoms (e.g., flat and circumstantial speech, occasional panic attacks) OR moderate difficulty in social occupational, or social functioning (e.g., few friends, conflicts with co-workers).
- **50-41:** Serious symptoms (e.g., suicidal ideation, severe obsessional rituals, frequent shoplifting) OR any serious impairment in social, occupational, or school functioning (e.g., no friends, unable to keep a job).
- **40-31:** Some impairment in reality testing or communication (e.g., speech is at times illogical, obscure, or irrelevant) OR major impairment in several areas, such as work or school, family relations, judgment, thinking, or mood (e.g., depressed man avoids friends, neglects family, and is unable to work, child frequently beats up younger children, is defiant at home, and is failing at school).
- **30-21:** Behavior is considerably influenced by delusions or hallucinations OR serious impairment in communication or judgment (e.g., sometimes incoherent, acts grossly inappropriately, suicidal preoccupation) OR inability to function in almost all areas (e.g., stays in bed all day, no job, home, or friends).
- **20-11:** Some danger of hurting self or others (e.g., suicide attempts without clear expectation of death, frequently violent, manic excitement) OR occasionally fails to maintain minimal personal hygiene (e.g., smears feces) OR gross impairment in communication (e.g., largely incoherent or mute).
- **10-1:** Persistent danger of severely hurting self or others (e.g., recurrent violence) OR persistent inability to maintain minimal personal hygiene OR serious suicidal act with clear expectation of death.
- **0:** Inadequate information.

California GAF to WPI table from the SCHEDULE FOR RATING PERMANENT DISABILITIES, January 2009: Psychiatric Impairment GAF to WPI Conversion

GAF=WPI	GAF=WPI	GAF=WPI	GAF=WPI	GAF=WPI	GAF=WPI	GAF=WPI
1 = 90	2 = 89	3 = 89	4 = 88	5 = 87	6 = 87	7 = 86
8 = 85	9 = 84	10 = 84	11 = 83	12 = 82	13 = 82	14 = 81
15 = 80	16 = 80	17 = 79	18 = 78	19 = 78	20 = 77	21 = 76
22 = 76	23 = 75	24 = 74	25 = 73	26 = 73	27 = 72	28 = 71
29 = 71	30 = 70	31 = 69	32 = 67	33 = 65	34 = 63	35 = 61
36 = 59	37 = 57	38 = 55	39 = 53	40 = 51	41 = 48	42 = 46
43 = 44	44 = 42	45 = 40	46 = 38	47 = 36	48 = 34	49 = 32
50 = 30	51 = 29	52 = 27	53 = 26	54 = 24	55 = 23	56 = 21
57 = 20	58 = 18	59 = 17	60 = 15	61 = 14	62 = 12	63 = 11
64 = 9	65 = 8	66 = 6	67 = 5	68 = 3	69 = 2	>70 = 0

THE SECOND CHALLENGE

- Many models of long COVID are based on the stress hypothesis, such that chronic disease is maintained by poor stress reactivity
 - This stress reactivity can be objectively identified through neuroimaging, biomarkers, and other diagnostic tests
- However, even in credible patients, the question remains to what degree is the disability linked to permanent impairment versus a treatable condition
- In a similar manner, how much of one's subjective impairment is psychological versus neurological?
 - Further complicated by the fact that psychological factors exacerbate health status in these patients!

THE WORK COMP “LOOPHOLE”

- MMI is a legal term used when an applicant is felt to no longer benefit from treatment through the WC system (usually within the next year)
 - “Permanent depression” is unlikely to be appropriate to say, but “MMI for depression” is an appropriate statement
- Thus, patients with persisting deficits that are intractable to treatment in the context of a credible applicant can be rated MMI for long COVID
- Patients who are working without restrictions most likely will obtain a WPI between 1-14% per the AMA guidelines
- More severe cases can exceed 14%

IN REALITY...

- It remains unclear the extent which long COVID will remain a public health crisis in the future
- Some argue the psychological factors exacerbate many long COVID cases
 - The iatrogenic effect (also seen with mild TBI)
 - Media misrepresentation of facts
 - General stress and trauma associated with the pandemic outside of actual disease
- In 10-20 years, will long COVID remain in the public eye and if it does not, will cases subsequently wither?

BEST PRACTICE

- 1. Record review to learn the facts of the case including signs that support or refute a purported long COVID diagnosis
- 2. Establish credibility with patient through performance and symptom validity tests
- 3a. If credible, interpret neurocognitive and psychological data to determine if there is objective evidence of cognitive/psychiatric dysfunction
- 3b. If not credible, interpret whatever data can be interpreted to establish reasons for poor credibility
- 4. Make diagnoses, treatment recommendations, ratings, apportionment

CASE STUDY I

- 40-year-old applicant catches COVID in January of 2021 (omicron variant)
- Mild case, stays at home, recovers but has persisting symptoms
 - Has not worked since infection
- Neurologist documents subjective headaches, dizziness, memory loss, rates 3% WPI for headaches and recommends neuropsychological testing
- Applicant fails effort measures; personality inventory supports a somatic symptom disorder
- WPI 0% for cognitive disability and 15% for psychiatric disability
 - Apportion 25% to preexisting psychiatric factors identified in deposition

CASE STUDY 2

- 62-year-old applicant catches COVID in August of 2021 (delta variant)
- Not hospitalized but does have shortness of breath, receives oxygen
- Persisting symptoms remain although the applicant is working full-time
 - Neuroimaging identifies white matter vascular abnormalities
- Credible on testing, has significant executive deficits on testing
- WPI is 12% for cognitive disability, 8% for psychiatric disability
 - Apportion 10% of cognitive disability to white matter changes

CASE STUDY 3

- 27-year-old catches COVID in January of 2022 (boosted, omicron variant)
- Mild-to-moderate symptoms that persist after illness, with autonomic dysfunction (nausea, vomiting, GI issues, headaches, dizziness, temperature regulation issues)
- Working but on restrictions per PTP
- Credible and has moderate deficits on measures of attention and memory
- WPI is 28% for cognitive disability and 15% for psychiatric disability
- No apportionment indicated

100% DISABILITY?

- Unlikely to emerge in mild-to-moderate cases
- Possible in severe cases where there is evidence for hypoxic/vascular neurological damage linked to COVID
- May be possible in severe psychiatric cases (conversion disorder or profound PTSD in which the patient cannot function in their basic ADLs)
 - Facts of the case will uphold this finding if true

THANK YOU!