NEUROPSYCHOLOGICAL SYMPTOMS IN POST-COVID CONDITIONS

MICHELLE HADDAD, PHD
DIRECTOR OF POST-COVID NEUROPSYCHOLOGY CLINIC
DIRECTOR OF INPATIENT NEUROPSYCHOLOGY
DEPARTMENTS OF REHABILITATION MEDICINE & NEUROLOGY
EMORY UNIVERSITY SCHOOL OF MEDICINE
POTENTIAL MECHANISMS OF DIRECT NEUROINVASION

• ACE2 is expressed in the nasal cavity epithelia, including that around the olfactory nerve
  – Current hypothesis is that SARS-CoV-2 may enter the brain through the olfactory nerve/bulb
  – Because ACE2 is expressed throughout the brain, this may be a direct avenue of infection

• Direct presence of virus in the brain suggested by presence of viral RNA in the CSF of some infected patients
  – The proposed route of transmission would be: nasal cavity > olfactory nerve > olfactory bulb > brainstem
  – This route of infection has been demonstrated in other strains of endemic coronaviruses
  – Importantly, however, it remains unclear whether the presence of viral RNA is associated with functionally-relevant damage

• Additional hypotheses – signaling across the blood-brain barrier

Source: Bougakov, Podell & Goldberg, 2020
INDIRECT IMPACTS ON THE BRAIN

• Hypoxic/Anoxic injury
• Vascular compromise
  • Stroke
  • Hypercoagulability
  • New possibility: Micro clots
• Inflammation
  • Edema
  • Encephalitis/Encephalopathy
• Autoimmune
• Metabolic dysfunction/Delirium

Source: Hewitt et al., 2021
BUT...

- The prevalence of self-reported brain fog does not correlate with hospitalization, treatment, or acute severity (as measured by ventilation status)

Source: Haddad & Truong, unpublished data from Emory University COVID Clinics
AMONG PATIENTS WHO SELF-REPORT BRAIN FOG...

• The most commonly described impairments are in:
  – **Memory**: 92.2%
  – **Attention**: 76.5%
  – Fluency: 29.4%
  – Executive Function: 25%

Source: Haddad & Truong, unpublished data from Emory University COVID Clinics
OVERALL, THE MOST COMMON IMPAIRMENTS ON OBJECTIVE TESTING ARE...

Auditory Processing Span

- Intact
- Borderline
- Mild
- Moderate

Auditory Dual Processing

- Intact
- Borderline
- Mild
- Moderate

Semantic Fluency

- Intact
- Borderline
- Mild
- Moderate

Phonemic Fluency

- Intact
- Borderline
- Mild
- Moderate

Source: Haddad & Truong, unpublished data from Emory University COVID Clinics
OVERALL, THE MOST COMMON IMPAIRMENTS ON OBJECTIVE TESTING ARE...

**Auditory Encoding**

- Intact
- Borderline
- Mild
- Moderate

**Auditory Retention**

- Intact
- Borderline
- Mild
- Moderate

**Problem-Solving**

- Intact
- Mild
- Moderate

Source: Haddad & Truong, unpublished data from Emory University COVID Clinics
ATTENTION

• Many patients have difficulty with sustained attention, particularly when there is also a speed component
• Working memory (ability to hold information in your mind and manipulate or work with it) is also very frequently impacted
• Remember, attention is important for EVERYTHING ELSE!
• Patients will often endorse “memory problems” when in fact what they are describing are attention problems
  • Losing track of tasks
  • Losing train of thought
  • Missing steps in a routine
COGNITIVE FLUENCY

• The ability to efficiently generate and articulate novel thoughts

• Many patients with PCC have diminished speed/efficiency of thinking

• Functionally, presents as feeling slow or confused
  • Taking much longer to complete familiar tasks
  • Struggling to find the right words (this is different from aphasia in that the patient IS able to get the words when given enough time)
LEARNING AND MEMORY

• Remember: Attention is the first part of learning/memory
  • Patients with impaired attention will VERY LIKELY also have impaired encoding of new information
• Poor encoding leads to transferring too little information into long-term memory
• But this is different from forgetting information that you DID encode
• Important to differentiate between encoding problems vs. retention problems since strategies are different
  • Most patients with PCC have difficulty with encoding, NOT retention
EXECUTIVE FUNCTIONING

• For most patients with attention problems, a further consequence is difficulty with planning and organization.
• If you can’t pay attention to all relevant details, it’s difficult to adequately plan, prioritize, etc.
• In a smaller proportion of patients, there is also difficulty with strategy generation and problem-solving.
• Patients will usually describe this as difficulty with making decisions, or others may identify it as errors in judgment.
  • For example, a supervisor at work may point out mistakes.
ADJUSTMENT-RELATED MOOD SYMPTOMS ARE VERY PREVALENT IN PATIENTS SEEKING CARE FOR PCC

• When asked about mood disturbance specifically around symptoms/current condition:
  • 82.4% reported anxiety
  • 68.6% reported depression

• Important to note, this is new-onset emotional distress

• Emotional reaction to a stressor can be perfectly appropriate and still have a significant impact on functioning

Source: Haddad & Truong, unpublished data from Emory University COVID Clinics
PSYCHOLOGICAL SYMPTOMS AND COGNITION

• Mood disorders are also associated with deficits in attention, fluency, learning/memory, and executive function

• Although psychological symptoms do NOT account for all post-COVID cognitive symptoms, they can certainly worsen functioning

• Vicious cycle of catastrophic thoughts is very common
  • Cognitive slip -> “my brain is broken, I’m such an idiot, I’ll never be the same again” -> distraction caused by catastrophic thoughts -> further cognitive slip -> further catastrophic thoughts -> and so on
  • In this cycle, it’s also very easy to discount good performance
NEUROPSYCHOLOGICAL DATA AREN’T EVERYTHING!

• Neuropsych assessment usually occurs under “ideal” circumstances

• Formal evaluation is intended to capture maximal cognitive ability (although it doesn’t always succeed at that)

• Of course, most daily activities don’t occur under these ideal conditions

• It’s important to consider how daily function might differ from a formal evaluation, and make recommendations accordingly
RECOMMENDATIONS

• Refer for neuropsych evaluation when possible
  • If not possible, consider how to ask about daily functioning in ways that differentiate between different cognitive domains
  • It isn’t enough to just ask about “memory problems” etc.

• For problems with attention, consider use of a stimulant or activating antidepressant

• Encourage organization, routine, and limitation of external distractors

• For problems with fluency, accommodations for extra time may be needed
RECOMMENDATIONS

• Pacing strategies can be very helpful, and should include mitigation of physical symptom impact

• Referral to Speech Therapy and/or Occupational Therapy for cognitive rehabilitation (learning compensatory strategies)

• Psychotherapy and/or medication management for mood symptoms

• Education on the relationship between catastrophic thoughts and cognitive function

• Maybe most importantly: Find a balance between validation of symptoms/life impacts and hope for improvement