



NEUROPSYCHOLOGICAL SYMPTOMS IN POST-COVID CONDITIONS

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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

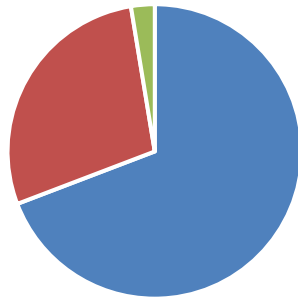
INDIRECT IMPACTS ON THE BRAIN

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

BUT...

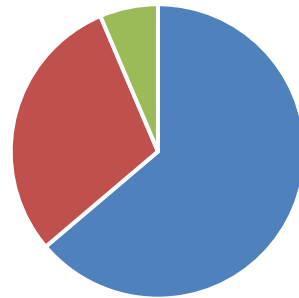
- The prevalence of self-reported brain fog does not correlate with hospitalization, treatment, or acute severity (as measured by ventilation status)

Reported Attention Problems



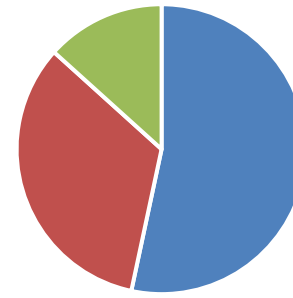
■ Mild ■ Moderate ■ Severe

Reported Memory Problems



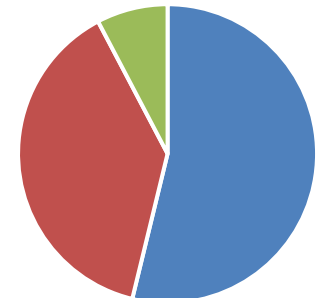
■ Mild ■ Moderate ■ Severe

Reported Fluency Problems



■ Mild ■ Moderate ■ Severe

Reporting Executive Dysfunction



■ Mild ■ Moderate ■ Severe

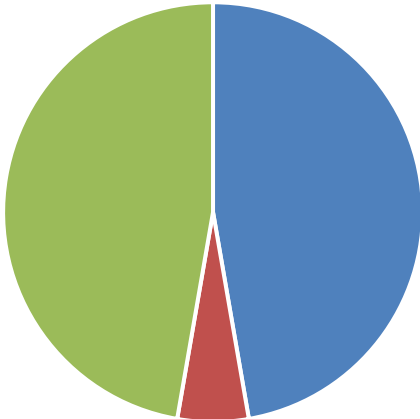
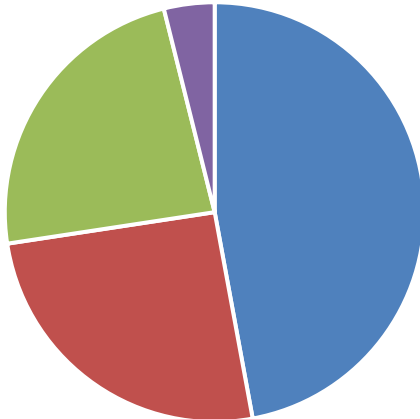
AMONG PATIENTS WHO SELF-REPORT BRAIN FOG...

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

OVERALL, THE MOST COMMON IMPAIRMENTS ON OBJECTIVE TESTING ARE...

Auditory Processing Span

Auditory Dual Processing

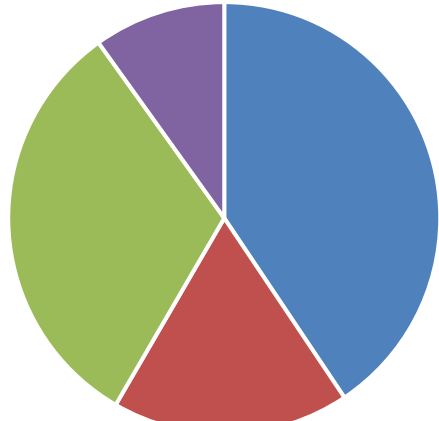
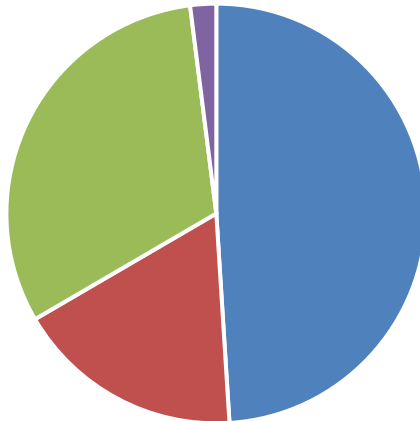


■ Intact ■ Borderline ■ Mild ■ Moderate

■ Intact ■ Borderline ■ Mild

Semantic Fluency

Phonemic Fluency

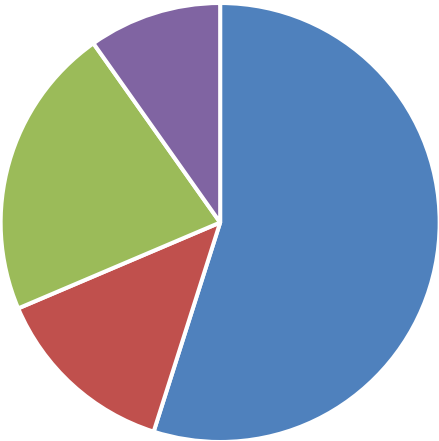


■ Intact ■ Borderline ■ Mild ■ Moderate

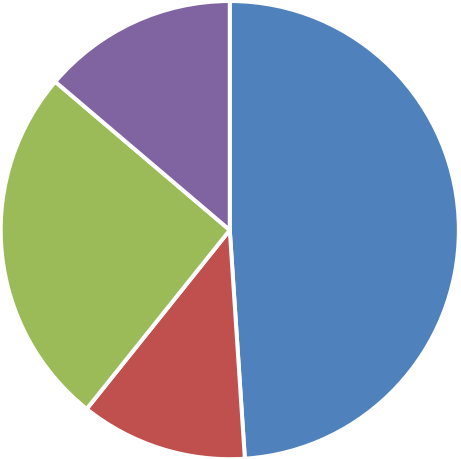
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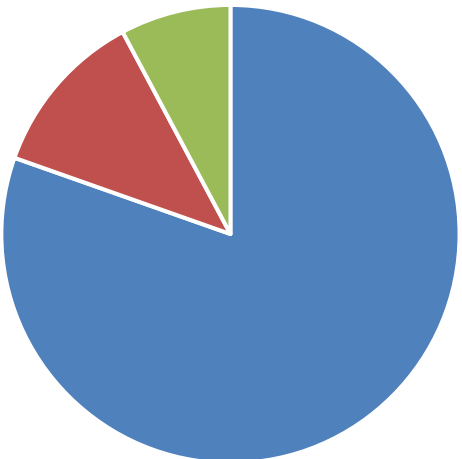
Auditory Encoding



Auditory Retention



Problem-Solving



■ Intact ■ Borderline ■ Mild ■ Moderate

■ Intact ■ Borderline ■ Mild ■ Moderate

■ Intact ■ Mild ■ Moderate

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

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