Brain-fog – side note or the main event?

Patrick Onions, June 2023

Covid fog is a condition that afflicts a significant proportion of people who have been infected with COVID, even mild cases. Symptoms can persist for several months after the initial infection has passed, and typically include problems with concentration, language fluency, processing speed, executive function, and working memory. Those afflicted can easily struggle to find words, become overwhelmed, embarrassed or irritable. Most researchers regard the cause to be neuro-inflammation and interference with neuro-transmission. COVID-19 activates brain cells called microglia, which release greater quantities of cytokines, and this impairs formation of neurons and cell communication. Instead of returning quickly back to normal, one cytokine in particular tends to remain elevated after many weeks. Unfortunately there does not appear to be a treatment; but coping may be easier with healthy living, simplifying situations, and applying some daily workarounds.

I blame my parents

My family tended to visit the doctor only when something was seriously amiss, and mental health was not on that list. Intrigued by those around who were “nuts” or a bit “loopy”, I can recall how neighbour John was found naked in the street, Uncle Ronnie had a “bad war” with two years in a Japanese POW camp, and Grandma enjoyed the gin a little too much. For the kids, Ritalin (or the strap) was a broad-spectrum cure-all for childhood behavioural issues. This upbringing left me well-prepared to deal with most traumatic injuries, but naïve and perhaps wilfully ignorant about mental health.

The brain and its functions are complex and hidden, and changes often occur at an imperceptible pace. Recognising problems requires some self-awareness and knowledge; a baseline to compare against, an understanding of what the symptoms mean, and the motivation to pay attention and not stick one’s head in the sand. Like boiling frogs, mental health issues may only be noticed when it is too late, and then only after causing some serious umbrage.

The onset of COVID fog was subtle, following closely on from the miserable respiratory infection, and by its nature suppressed any mindfulness. Throughout there was this vague sense of something being wrong, but in lacking the ability to recognise changes in behaviour it took me five months to do something about it. I may not have been able to alter my physiological state, but coping mechanisms could have been put in place much sooner.

More than just the sniffles

Annual leave in December me to recover from a mild dose of COVID. Pottering around the house was not an intellectual challenge, so I was not aware of any cognitive issues. Even on returning to work any symptoms were easily dismissed. Over the course of a month things worsened, although without causing me any alarm. Fuzzy, forgetful and easily distracted, there were days when my speech was inarticulate. Creativity withered, thoughts became muddled and aimless, and conversations soon forgotten. Any conscious awareness that a situation was brewing took three months, and only then when triggered by the realisation that I was working weekends to catch up on work not completed.

COVID-19 can damage the brain in many ways. The "fog" I was experiencing is quite distinct from more severe conditions, such as encephalitis, strokes and hypoxia [1]. COVID fog is also known as "brain fog" and "cognitive impairment". It presents as a range of symptoms including problems with attention, category fluency, concentration, confusion, executive function, language fluency, phonemic fluency, processing speed, word-finding, and working memory [2, 3, 4, 5, 6].

Alongside COVID fog, patients may display an extensive range of neurological, neuromuscular, psychological and social symptoms. These include anxiety and depression [5], feelings of being overwhelmed when faced with complex situations [3], feelings of guilt and shame and no longer trusting one's own brain [7], and reduced quality of life [5, 6].

COVID is more than just a cough and loss of taste, and fog is quite prevalent and even appears in mild cases [8]. Occurrence may range from one in four patients [4], a third of patients with long-COVID [9], to as many as 88% of patients suffering from long-COVID [7]. Memory impairment was reported in one study as 16% of non-hospitalised and 35% of hospitalised patients, and concentration impairment in 26% of cases [5]. Analysis of published research found a median of 20% of cases showing cognitive deficit and 28% showing memory loss, about half the number displaying shortness of breath [10].

These symptoms are persistent too. Nearly a third of COVID fog cases last beyond the acute stage of infection[1] [10]. Many will experience fog up to several months after recovery [2, 7, 5], and it may appear to fluctuate or even relapse [6].

Long-COVID research suggests some people will be at greater risk of catching that disease, with implications for the likelihood of experiencing fog. Risk factors include the female gender [5, 11, 12], increased age [5, 11], and minority ethnicity [5]. Pre-existing conditions can increase risk too; such as respiratory, gastrointestinal, existing depression or anxiety, seasonal allergies, and particularly autoimmune conditions [13]. Interestingly, graduates and urban residents may be at lower risk [11].

It is notable too that brain fog symptoms are not unique to COVID. Strong similarities to "chemobrain" have been observed [8, 4], and concentration and memory difficulties are associated with H1N1 influenza [8]. Historical evidence exists of psychoses associated with the Russian influenza of the 1890s and Spanish flu in 1918 [14]. Similar symptoms can also appear in cases involving CD200 degradation, CFS, diphtheria, ME, PTS, and even severe fatigue [15, 7, 12].

What's wrong with me

The irony of delving into the causes of COVID fog isn't lost on me. The average neuroscience paper is not light reading, and the acronyms and depth of knowledge needed will throw up an impenetrable mental jungle. Still, persistence in finding a logical explanation was needed because the alternative would be, to paraphrase Arthur C. Clark, to regard COVID as "indistinguishable from magic" [16].

Explained simply, many researchers believe brain fog is triggered when COVID challenges the immune system. Brain cells called microglia become activated, they release unusual quantities of chemicals called cytokines, and this signals an inflammatory response throughout the brain

[1] A patient can experience COVID in stages; starting with *acute*, on to *post-acute* where symptoms continue beyond 3 weeks, and *long* or *chronic* continuing beyond 12 weeks following the start of symptoms. These periods are indicative and not universally agreed.

[6, 17, 4]. This neuroinflammation impairs the formation of neurons (neurogenesis) and affects the myelin membranes associated with cell communication. In the case of COVID, the levels of cytokines remain high and microglia continue to be activated [8, 4].

Microglia are immune cells in the central nervous system that are involved in brain development, network maintenance and injury repair [17]. They are also involved in cognitive processes, pruning of weak synapses, cell communication, control of scale of neural activity, and pain amongst other functions. Microglia are naturally non-activated, but are highly sensitive and change their function in response to a wide range of stimuli reaching their receptors. This generally occurs with age, disease, and degradation of stabilisers like the surface membrane glycoprotein CD200 [17, 18].

Microglia responses include releasing immune-transmitters such as cytokines. Some level of cytokines are necessary to maintain homeostasis – or balance - in the brain [18]. However, COVID-19 elevates these [8], which further activates microglia, and this impairs neurogenesis and affects the myelin membranes associated with cell communication [19]. One cytokine in particular (CCL11) tends to remain elevated after many weeks, explaining symptoms and their persistence [4, 8].

There may be other explanations for COVID fog. One alternative is that the pre-frontal cortex becomes affected by a reduction in calcium regulation and opening of potassium channels, which leads to reductions in synaptic firing and consequential issues with working memory [3]. Another study [6] hypothesised that COVID fog could be due to – in addition to the neuro-inflammation and "*ongoing activity of primed immune cells*" described by other researchers - direct viral damage, clotting issues, dysfunctional nerve signalling, autoimmunity, cell damage and other mechanisms. No corroborating studies were found for these recent papers.

Treat it, or just deal with it

The expression "time is a great healer" is of no comfort at the moment. Lacking any approved treatments [3], and with the waiting list at my General Practitioner being about 6 months, I've had to muddle through by gravitating toward three coping mechanisms; living (more) healthily, managing situational anxiety, and working around the limitations this imposes.

Healthy living means doing things in moderation. Aerobic exercise, good food, avoiding alcohol and drugs, sleeping well, socialising and cognitive exercises like reading are all known to aid cognitive processes [1]. It probably doesn't help to start the day with two large mugs of coffee, but that has been the only way to keep the inner zombie in check.

Managing situational anxiety has been a real struggle. Moving into an unfinished house whilst holding down a full-time job was not helpful as it created an unsettling distraction. Work projects were a bit chaotic too, with lots of "bitty" tasks that required constant mental gymnastics. The only way to cope has been to eliminate uncertainty as quickly as possible, by wilfully prioritising and breaking the large and complex tasks down to eat the proverbial elephant bite by bite.

Working around the limitations that brain fog imposes is easier said than done. Lists of everything will come in handy, post-its are essential, and taking copious notes is the only way I can remember conversations even later the same day. Concentrating on a single problem for more than 30 minutes is still impossible, and it can be very counter-productive to doggedly push myself to complete something. It helps to switch between tasks requiring different skills, thereby giving my brain a break whilst still remaining productive. It also helps to work on paper

rather than staring at the screen, either by printing out a document for editing or drawing on a large A3 sheet.

Managing a long day is important too. Anyone who has known somebody with dementia will recognise the late-day confusion known as “sundowning”. A reliable solution is to take the dog for a walk late afternoon, find some food, and return to the desk for a couple for hours early evening. The final chore is to list tomorrow’s priorities and review today’s achievements, rewarding myself and reminding me I am not totally useless.

Recently the symptoms have started to subside. Perhaps the problem has run its course, maybe it is summer and a good dose of Vitamin D has worked, or maybe the antihistamines for hay-fever are subduing the immune system. All I know is that five months has been way too long to feel this way.

Some big words

CFS	Chronic fatigue syndrome
comorbidity	When two or more independent conditions are present in the same person at the same time.
COVID fog	A colloquial term that refers to a range of symptoms [4] that may be categorised as cognitive impairment ([2, 3]
COVID phases	Stages that a patient can experience; starting with *acute*, *post-acute* where symptoms continue beyond 3 weeks, and *long* or *chronic* continuing beyond 12 weeks following the start of symptoms.
COVID-19	(COronaVIrus Disease 2019) is a highly contagious disease caused by the SARS-CoV-2 strain of coronaviruses.
executive functions	Cognitive processes such as multi-tasking, focus and concentration.
homeostasis	A process of self-regulation whereby an organism keeps its functions in balance
ME	Myalgic encephalomyelitis
microglia	The primary immune cells in the brain.
myelin	A specialised membrane for cell communication
Neurogenesis	The process of forming new neurons in the brain.
Neuroinflammation	A process triggered by an attack on the immune system
PASC	Post-acute sequelae of COVID-19.
prefrontal cortex	(PFC) A frontal area of the brain that manages executive functions, working memory, personality expression, speech and language.
PTS	Postural Tachycardia Syndrome

Smarter people than me said it

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