SARS-CoV-2 and Toxoplasma gondii shared symptoms suggest muscle cells and neurons are their chronic infection reservoirs

Kevin Roe

Received: 22 September 2022 / Accepted: 5 October 2022 / Published online: 10 October 2022
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Keywords Brain infections · Long COVID · SARS-CoV-2 · Latent infections · Toxoplasma gondii

A significant percentage of COVID-19 patients experience extended duration Long COVID [1, 2]. Several symptoms have been exhibited in Long COVID patients, such as mental dysfunctions (e.g., cognitive dysfunction, altered mental status, mental confusion or behavioral changes), neurological deficits (which along with depression, anxiety, memory and attention deficiencies, sleep disorders may alternatively be classified under mental dysfunctions), movement abnormalities (e.g., involuntary movements or ataxia/incoordination), fatigue, fever, dyspnea (labored breathing), myalgia (muscle pain), arthralgia (joint pain), tinnitus (ear ringing), vertigo (dizziness), otalgia (earache), anosmia (impaired smell), dysgeusia (impaired taste), speech and swallowing deficits and hair loss [1–4].

The primary aim of this letter is discuss some considerable similarities between the symptoms of Long COVID and the symptoms resulting from infections by the protozoan parasite Toxoplasma gondii. Table 1 provides a comparison of several potential symptoms that can result from infections by these pathogens.

Several Long COVID neurological symptoms could potentially be explained by cranial nerve (C.N.) infections affecting the functions of the 12 cranial nerves [4–6]. Another paper has proposed a link between Long COVID and the SARS-CoV-2 full spike protein through induced neuroinflammation [7]. Additionally, a study of SARS-CoV-2 antigens and cytokines from plasma samples extracted from 63 adults previously infected by SARS-CoV-2, including 37 adults diagnosed to have Long COVID/post-acute sequelae of COVID-19 (PASC), detected the SARS-CoV-2 full spike protein in 60% of individuals exhibiting Long COVID/PASC symptoms up to 12 months past their COVID-19 diagnosis [8]. This suggested to the researchers that there is a viral chronic infection reservoir for SARS-CoV-2, causing Long COVID/PASC in at least 60% of the cases [8]. However, the S1 and N proteins of SARS-CoV-2 were detected in fewer individuals and several inflammatory cytokine blood plasma levels were inconclusive [8]. The researchers hypothesized a viral reservoir of chronic infection and suggested that since Long COVID/PASC is a heterogeneous syndrome, that this could depend on the viral reservoir tissue location [8]. This raises several questions: (1) is there a viral reservoir causing 60% of the Long COVID/PASC cases, (2) where is the viral reservoir located and (3) are there other pathways without a viral reservoir for the other 40% of the Long COVID/PASC cases?

The virus SARS-CoV-2 is not the only pathogen capable of chronic infections exhibiting numerous neurological and psychological symptoms. Protozoan parasites, including Toxoplasma gondii, cause chronic infections which in some cases can exhibit neurological and psychological symptoms that almost parallel Long COVID/PASC [6].

Since these pathogens are pervasive and adept intracellular pathogens, it is plausible that SARS-CoV-2 and T. gondii could in some cases use central nervous system neurons and/or muscle cells as chronic infection reservoirs. This could also explain the major similarities in these pathogens regarding the symptoms observed during their potentially chronic infections.

Long COVID/PASC symptoms also extensively match many of the symptoms caused by a partially or fully reactivated T. gondii infection [6]. Individuals infected by T. gondii can exhibit an extensive number of neurological and muscular symptoms, such as altered mental status, focal neurological deficits, mental confusion, cognitive dysfunction, ataxia, behavioral or psychomotor changes, involuntary movements, dyspnea, fevers, seizures, headaches, changes in...
vision, pneumonia, chorioretinitis and various cranial nerve infections [4, 6].

*T. gondii* has a documented capability to maintain chronic infections in muscle cells and central nervous system neurons with intracellular bradyzoite cysts [6]. Intracellular infections of cells typically lead to pathogen antigen presentation by the infected cells to CD8 T cells to induce cytotoxic CD8 T cell attacks to limit cellular infections [6]. However, neurons are known to be immuno-privileged to minimize damage from inflammation and other immune responses [9]. In addition, quiescent muscle cells, such as muscle stem cells, are also immuno-privileged with down-regulated antigen presentation [10]. Therefore, some adept pathogens would seek to evolve means to evade or disable CD8 T cells, such as *T. gondii’s* use of metabolically inactive bradyzoite cysts in neurons and muscle cells, to evade cytotoxic attack by CD8 T-cells and maintain chronic infections [6].

Such chronic infections of neurons by *T. gondii* cysts can also potentially disrupt brain levels of neurotransmitters including glutamate, gamma-aminobutyric acid (GABA), and dopamine [6]. These disruptions can explain why latent *T. gondii* infections in some cases are linked to an extensive number of brain-associated disorders [6].

Coronaviruses, including the SARS-CoV-2 virus, can in some cases penetrate the blood–brain barrier (BBB), and/or utilize a neuronal pathway via sensory nerves (e.g., the olfactory nerve) or motor nerve endings [6]. The extent of transport of SARS-CoV-2 into the brain via the BBB or nerve pathways, can cause different infection pathways and consequences, and could potentially explain why Long COVID/PASC has widely varying sets of observed symptoms among individuals. There may also be other pathways without a chronic infection viral reservoir that could explain the remaining Long COVID/PASC cases that lack SARS-CoV-2 antigens.

In conclusion, the post-infection symptoms of Long COVID/PASC are sometimes experienced after active SARS-CoV-2 virus infections. Long COVID/PASC exhibits several neurological and muscular symptoms that substantially parallel *T. gondii* infection symptoms. *T. gondii* is known to use central nervous system neurons and muscle

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**Table 1** Compares the symptoms of Long COVID/PASC and *T. gondii* infections

| Exhibited Symptoms 1 | Long COVID | *T. gondii* | Alternative Category Or Possible Causation |
|---------------------|------------|-------------|------------------------------------------|
| Mental Dysfunctions 2 | Observed | Observed | cognitive dysfunction, altered mental status, mental confusion or behavioral changes |
| Neurological Deficits | Observed | Observed | mental dysfunctions? |
| Depression | Observed | Possible | a mental dysfunction? |
| Anxiety | Observed | Possible | a mental dysfunction? |
| Sleep Disorders | Observed | Possible | a mental dysfunction? |
| Movement Abnormalities 3 | Observed | Observed | involuntary moves or ataxia/incoordination |
| Fatigue | Observed | Observed | from chronic infection? |
| Fever | Observed | Observed | from chronic infection? |
| Hair loss | Observed | Possible | from chronic infection? |
| Dyspnea/Labored breath | Observed | Observed | from muscle cell infection? |
| Myalgia/Muscle pain | Observed | Possible | from muscle cell infection? |
| Arthralgia/Joint pain | Observed | Possible | from joint/muscle cell infection? |
| Tinnitus/Ear ringing | Observed | Possible | cranial nerve infection |
| Otalgia/Earache | Observed | Possible | cranial nerve infection |
| Vertigo/Dizziness | Observed | Possible | cranial nerve infection |
| Anosmia/Impaired smell | Observed | Possible | cranial nerve infection |
| Dysgeusia/Impaired taste | Observed | Possible | cranial nerve infection |
| Speech & Swallow Deficits | Observed | Possible | cranial nerve infection |

1[Refs 1–6]
2Mental dysfunctions include cognitive dysfunction, altered mental status, mental confusion or behavioral changes, neurologic deficits are perhaps a duplicated category; depression and anxiety could also be duplicated categories of mental dysfunctions
3Movement abnormalities include involuntary movements and ataxia/incoordination
cells to maintain chronic infections. It is therefore plausible that in some cases SARS-CoV-2 and *T. gondii* both use central nervous system neurons and muscle cells as reservoirs to maintain chronic infections. There may also be other pathways without a chronic infection viral reservoir that could explain the remaining Long COVID/PASC cases that lack SARS-CoV-2 antigens.

**Acknowledgements**  There are no acknowledgments.

**Funding**  This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Data availability**  Data sharing is not applicable to this article as no new data were created or analyzed in this study.

**Declarations**

**Conflict of interest**  The author has no potential conflicts of interest.

**Ethics statement**  The author confirms that the ethical policies of the journal, as noted on the journal’s author guidelines page, have been adhered to. No ethical approval was required as this is an article with no original research data.

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