Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Hypothesized behavioral host manipulation by SARS-CoV2/COVID-19 infection

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ABSTRACT

Although not widely studied, behavioral host manipulation by various pathogens has been documented. Host manipulation is the process by which a pathogen evolves adaptations to manipulate the behavior of the host to maximize reproduction (R_o) of the pathogen. The most notable example is rabies. When a host is infected with the rabies virus it gets into the host's central nervous system and triggers hyper aggression. The virus is also present in the rabid animal's saliva so being bitten transmits the infection to a new host and the old host is left to eventually die if untreated. Toxoplasmosis is another example. When mice are infected they demonstrate a fearlessness toward cats, thus increasing their chances of being eaten. Toxoplasmosis needs the digestive tract of the feline to survive. Recent studies have shown that exposure to toxoplasmosis in humans (e.g., through cat feces) has also been associated with behavioral changes that are predicted to enhance the spread of the pathogen. Even the common influenza virus has been shown to selectively increase in-person sociality during the 48-hour incubation period, thus producing an obvious vector for transmission. Here we hypothesize that the novel coronavirus, SARS-CoV2, which produces the COVID-19 disease may produce similar host manipulations that maximize its transmission between humans.

Introduction

For viruses to spread, being transmissible is essential. Survival is the most critical goal for different pathogens and parasites, especially concerning their chances of reproduction. Past research has shown that behavioral host manipulation can occur to promote the best interest of the pathogen [1,2]. Host manipulation can be viewed as adaptations that commandeer the behavior and actions of the host in ways that promote the reproductive best interests of the virus. Benefits may result in increased chances of transmission and survival. Host manipulation has been recognized in a number of pathogens such as toxoplasmosis, rabies, and influenza [1,2,3,4,5,6]. It is important to mention that certain pathogens are neuro-invasive, and understanding how it targets and manipulates the central nervous system (CNS) can broaden possible questions about host manipulation [7,8].

Focusing on how pathogens may impact individuals' behavior as hosts can also have important implications for the spread of epidemics and pandemics. Seeing increases in stress and various mental illnesses' may also be likely [5,9,10].

Behavioral manipulation can occur at different times of the pathogen's infection lifecycle. Here we outline a series of hypotheses that may present behavioral changes before transmission, during incubation, and before symptoms occur.

The hypotheses laid out here include, but are not limited to:

- Possible behavioral changes in humans that could promote the transmission of SARS-CoV2 prior to showing symptoms
- Possible changes in infected children that function to increase the risk of infection in older people such as parents and caretakers
- Possible long-term changes in unborn children
- Possible mutations that could drive further transmission

Hypothesis 1

Here we outline how the virus might promote social contact among those infected but remain asymptomatic during the incubation period. The current incubation period for SARS-CoV2 has been estimated at 5 days, but has been observed with a range between 0 and 24 days. It might be the case that incubation period is facultatively responsive to the possibility of transmission rate and R_0. In other words, with a high possibility of transmission, incubation to infection may be delayed in order to maximize number of hosts.

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An alternative means by which a virus could increase sociality is to reduce the negative emotional consequences of social exclusion. Several studies have documented that social exclusion produces the feeling of "pain", discomfort, and loss of self-esteem in humans [11]. This effect is magnified by the possibility of kin relationships [12]. The neural underpinnings of this social pain/neural alarm system appear to be located in the anterior cingulate cortex (ACC). If a virus could manipulate the response of the ACC to social exclusion (i.e. social distancing) people would feel less upset and might thus seek additional social support or simply gather socially (e.g., parties). In other words, if your primary friend group excludes you, you might find yourself seeking new people to "hang out" with instead of simply wallowing in your own discontent.

Hypothesis 2

There is some evidence that P.A.N.D.A.S. (pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection) produces increased separation anxiety in young children, along with obsessive compulsive behaviors [13]. These separation anxieties could promote infection of older hosts. Children have been reported to be fearful of being away from their primary caregivers - expressed as separation anxiety about being isolated from them for extended periods of time. If children become asymptomatic carriers of this virus, then they could function as strong vectors for transmission.

Hu et al. recently investigated 71 cases involved with pneumonia developing from the novel SARS-CoV2 virus [14]. It was found that many patients had low levels of serum cholesterol compared to 80 healthy controls. Total cholesterol, LDL-cholesterol, and HDL-Cholesterol were found to be significantly lower. Looking deeper into low cholesterol levels, Huang et al. found that lower serum cholesterol levels might correlate with depressive and anxious patients [15].

Hypothesis 3

There is mounting evidence in support of the idea that children born to mothers infected with various pathogens are at heightened risk of later complications, both physical and psychiatric. Most notably, children born to mothers that have been infected with the seasonal influenza virus show an increase in the incidence of schizophrenia and affective disorders [16,17,18]. The best estimates are that children born to mothers infected with influenza have a 4 times greater risk of developing either schizophrenia or an affective disorder, with schizophrenia being more likely. This line of research is still preliminary and controversial. We will not be able to observe the effects of SARS-CoV2 on unborn children for some time, but the possibility that this virus manipulates fetuses for its own reproductive success is not out of the question. For example, fetal exposure could produce an early immunological response that results in a suppression of symptoms, but not the elimination of infection nor behavioral changes that could later promote reemergence. Thus, these individuals could be very powerful vectors for transmission in the future. This is of course conjecture, but not outside the realm of possibility.

Hypothesis 4

Perhaps the biggest threat associated with this or any virus, is mutation that 1) becomes even more easily transmissible to others and 2) becomes rapidly lethal after the incubation period. Signs of the novel virus SARS-CoV-2 mutating are already being observed [19]. There appears to be a larger divergence between the novel SARS-CoV2 virus and other known coronavirus'. Researchers also found that the virus has branched into at least two types, type L and type S, in which the S is portrayed as the ancestral version of the SARS-CoV-2. Type L is known to be more prevalent and more aggressive, which could lead to a quicker spread throughout the populations.

Considerations

According to the World Health Organization, approximately 50% of COVID-19 cases are asymptomatic. This in itself can produce an increased opportunity for transmission; as individuals who are told to stay home are less likely to comply. Social isolation can fundamentally make people desire to be around others as well. The longer people are isolated, the more individuals will feel the need to interact with other people. It should also be considered that individuals with severe depression or suicidal tendencies may be at an increased risk of seeking social interaction as a means to execute their suicidal plan.

Furthermore, younger individuals who carry the virus but are not showing symptoms are able to transmit the virus more easily because adults are not taking the same precautions they would if the younger individuals were visibly sick.

Possible ways to collect data to test these hypotheses

If our hypotheses that this particular virus manipulates hosts during the incubation period to increase transmission, particularly if it makes them more social, then those who chose to go on spring break (or other vacations) should have a higher rate of infection than those who did not. This could seemingly be tested by examining spring break participation by those who test positive for COVID-19 or by looking at differences in viral status by comparing those who traveled somewhere vs. those who did not. There have been reports of young people holding so-called "coronavirus parties" of which at least one college-aged individual has become sick as a consequence. Some countries are making it illegal to purposefully congregate in a manner that would increase the odds of transmission. Making it illegal may actually promote these parties as young, already risky adults may blatantly ignore those laws. Obviously, these data are not ideal and have several confounds associated with them, but might provide initial insight into possible behavioral mechanisms at play.

Looking at occupational behaviors may be another possible means of data collection. Taking a measure of when people began to stay at home could be used to represent this. Those who are infected would be expected to have continued to work as a possible mechanism to further the spread of the virus.

Furthermore, for epidemiological purposes, Iceland is attempting to test the entire country for COVID-19. The data that comes from this will be very useful in examining the effects of the virus across various samples within the population. It would be ideal if, in addition to virological and biological data, Iceland (and other countries) were to collect behavioral data.

Conclusion

We want to make it clear that there are currently no known behavioral host-manipulations associated with SARS-CoV2/COVID-19 infection. The hypotheses laid out here were extrapolated from the well-known effects of other infections to change behavior as an adaptation to maximize the pathogens reproductive best interests. Although these are just hypotheses, only time will tell how SARS-CoV2 manipulates its host for its own survival and replication. Although some might presume that these scenarios are unlikely, it's our position that these hypotheses are worthy of serious attention.

Declaration of competing interest

The authors have no conflict of interest associated with this paper.

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