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Opinion

Neuroethical and Societal Challenges of 21st Century Epidemics

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Neurologic and neuropsychiatric manifestations of COVID-19 are affecting a growing number of people worldwide. We provide a brief overview of these manifestations, contrasting them with those of other 21st century viral epidemics, as well as mitigation strategies, and societal and moral considerations related to the pandemic. We highlight unique concerns relating to COVID-19 given the scale of infection, mental health challenges faced by health care providers and the general public, and the unprecedented social consequences, including benefits and possible harms associated with continuous connectedness using modern digital communication.

A New Normal

At the time of this writing, there are more than 37 million confirmed cases of Coronavirus Disease 2019 (COVID-19) worldwide. The pandemic has drastically altered daily life and is reshaping society as people navigate previously unimaginable challenges to personal, family, professional, and community safety. Alongside the well-recognized respiratory effects of COVID-19 are neurologic [1] and neuropsychiatric ones [2] that have been given less attention in the academic literature and public sphere, and the intersections between the neurologic effects and the neuroethics implications of the pandemic have been scarcely considered.

Here we reflect on lessons learned from this pandemic and other 21st century viral epidemics and suggest how these insights may be used to better plan for future ones. Alongside the far-reaching practical challenges and critical health care decisions that all pandemics have raised, involving, for example, access to health services, information dissemination, and support systems, are trade-offs and, at the heart of them, ethical and moral issues. Many involve balancing mental well-being on the one hand, with individual and collective responsibility on the other. This trade-off is exemplified by the practice of self-isolation that helps to reduce spread of infection, but comes at a personal cost. Unlike in most previous epidemics, some of the challenges associated with self-isolation are mitigated by the widespread use of modern digital communications technologies. No doubt, these new capabilities bring with them the enormous benefit of keeping people connected, but the double-edged sword lies in the unknown impacts of exposures to unprecedented amounts of screen time, not only on the developing brain of children, but on users of all ages along the lifespan.

Viral Epidemics and the Brain

To understand the neurological correlates of 21st century pandemics, we retrieved English language articles using the term 'neuro' from the Center for Disease Control COVID-19 database (11 May 2020). We reviewed 74 articles that met our criteria from a total of 427.

When comparing 21st century pandemics and epidemics, we find both common and distinct neurological phenomena (Table 1). Common to many of them are headaches and changes in

Highlights

A range of new ethical concerns accompanies the neurological and neuropsychiatric manifestations of COVID-19 compared with neuro-related symptoms and sequelae of past 21st century viral epidemics and pandemics.

The unique concerns of COVID-19 can be attributed to the scale of infection, mental health impacts, and access to digital communication technology.

Anxiety associated with the ethical and moral complexities of caring for patients, triaging them during a pandemic, and anticipating surges in cases may be as detrimental to the mental well-being of frontline health care workers as post-traumatic stress.

Previous recommendations for use of digital technology, especially among children, are being reconsidered in light of the demands for remote school, work, and socialization during the pandemic.

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Table 1. Overview of Neurologic Manifestations of 21st Century Pandemics and Epidemics

Pandemic/epidemic, years	Geographic region affected	Primary organ systems (in alphabetical order)	Common neurologic manifestations	Uncommon neurologic manifestations	Single case reports	Refs
COVID-19 2019–present (pandemic)	Worldwide	Gastrointestinal Neurologic Respiratory	Altered mental status Anosmia and hyposmia Decreased level of consciousness Dizziness and headache Generalized weakness	Cerebrovascular disease Encephalitis Encephalopathy Guillain-Barré Myelitis Seizures	Acute cerebellitis Acute necrotizing encephalopathy syndrome Generalized myoclonus Miller Fisher syndrome Postural tachycardia syndrome	[1,15–31]
Ebola 2014–2016 (pandemic)	Sub-Saharan Africa	Gastrointestinal Hematologic Neurologic Ophthalmologic	Altered mental status Decreased level of consciousness Generalized weakness Headache	Cranial neuropathies Dyesthesias/sensory neuropathies Memory loss Meningitis or encephalitis Seizures	Cerebrovascular disease Myoclonus	[32,33]
Middle East respiratory syndrome 2012–2020 ^a (pandemic)	Arabian peninsula	Cardiovascular Gastrointestinal Hematologic Neurologic Renal Respiratory	Altered mental status Ataxia Decreased level of consciousness Focal motor deficit	Cerebrovascular disease Encephalitis Neuropathy Paralysis	Necrotizing encephalopathy	[1,20,30,34,35]
Severe acute respiratory syndrome 2002–2004 (pandemic)	Worldwide	Respiratory Gastrointestinal Neurologic	None	Cerebrovascular disease Polyneuropathy	Encephalitis Encephalopathy Meningo-encephalitis Seizures	[1,20,36,37]
H1N1 2009–2010 (pandemic)	Worldwide	Gastrointestinal Neurologic Respiratory	Altered mental status Decreased level of consciousness Headache Paresthesias	Aseptic meningitis Cerebrovascular disease Encephalitis Encephalopathy Guillain-Barré syndrome Polyneuropathy Seizures Myelitis	Ataxia Focal status epilepticus Myoclonus Paralysis Vertigo	[38–42]
Zika 2013–2016 (epidemic)	Pacific Islands South America Southeast Asia	Hematologic Neurologic Fetal	Guillain-Barré syndrome Headache Microcephaly	None	Acute disseminated encephalomyelitis Sensorineural hearing loss Meningo-encephalitis Myelitis	[19,43–47]

^aOngoing but no longer considered a pandemic.

mental state and level of consciousness. Less prevalent, but shared across some of the epidemics, are various types of cerebrovascular disease, seizures, and encephalitis. Some neurological conditions are specific to one or two of the epidemics/pandemics or have been reported in case studies but their prevalence remains unclear.

We also identified commonalities in public health responses and mitigation strategies to these various epidemics/pandemics, including quarantine, isolation of vulnerable populations, and vaccination programs when available [3–5]. Notably, face covering was an adjunct, but not a central part, of the public health response in most prior pandemics, as the efficacy had not been proven by large-scale studies. The scale and global impact of COVID-19 is unique,

however, with the extent of physical distancing required and the enormous impact on different health systems and economies worldwide.

Dilution and diversion of health care resources are key challenges in any epidemic but can have especially devastating effects on neurologic and neuropsychiatric conditions. For example, delays in the administration of tissue plasminogen activator (TPA) for acute ischemic stroke can lead to long-term disability or even death. Delays in the adjustment of implanted neuromodulatory devices, available since FDA approval in the early 2000s for advanced Parkinson's disease, can interfere with their beneficial effects and similar considerations apply to neuromodulatory or neurosurgical treatments for drug-resistant epilepsy. Delays in perinatal care can have a profound impact on brain development, including deferred care for hydrocephalus and other brain malformations caused by the Zika virus. People with neurodegenerative diseases such as Alzheimer's have been overwhelmingly placed at risk in care facilities. The impact of deferred screening or diagnosis of many other neurologic conditions, including, for example, intracranial tumors that depend on timely diagnosis and treatment, is currently unknown and requires further epidemiological study.

The Grip of Uncertainty

An effective collective response to COVID-19 relies in large part on a cadre of experts who can make difficult public health decisions based on the best available evidence, including the experience of past pandemics. The operationalization of these decisions, however, relies on the concerted efforts of both the general public and frontline health care workers. This creates an ethical dilemma where public health decisions are largely utilitarian, in that they are made for the greater good, but they may have disproportionately negative effects on the very people who must implement them. In this regard, post-traumatic stress has been well documented after past epidemics [2,6,7]; COVID-19, however, may also bring to bear not only post-, but antecedent neuropsychiatric effects.

As two of the authors (C.F. and J.I.) discussed in the Royal Society of Canada Zero Canada COVID-19 series (<https://rsc-src.ca/en/voices/hidden-risks-pre-traumatic-stress>), the negative impact from anticipating surges of patients of unknown size and location, and accompanying moral dilemmas, may be as difficult as surviving them. As if this challenge alone was not enough, it exists against a well-documented backdrop of already existing fragilities of mental health among frontline health care workers [8,9]. Recognition, awareness, and attention to this extra layer of complexity imposed by COVID-19 can inform ethically grounded strategies to mitigate it. We see intersecting responses possible at both the level of health care systems and at the level of individual clinicians: identifying workers at high risk based on personal or occupational factors, directing them to care, encouraging positive and culturally relevant coping mechanisms, and reducing, to the extent possible, occupational stressors such as long working hours.

The COVID Connectome

COVID-19 struck the world in the modern age of technology that, for better and for worse, has created a flood of information, an infodemic [10], and, with it, extensive internet-enabled engagement. The confluence of these forces has enabled people to remain socially connected while physically apart, created both opportunities for intervention as they pertain to the brain and mental health, and raised some new ethical dilemmas as well.

No doubt, evidence-based guidance is essential for good public policy and access to it is largely online today. There is no shortage of resources to pull from for information and there is a continuous push of information through email and social media. During this pandemic and the associated lockdowns, children, youth, and families have turned to digital media to stay engaged and

connected. However, the benefits of online engagement must be balanced with the potential impact it may have on development, as well as the safety and well-being of users. Prior to the pandemic, the American Academy of Pediatrics, among other professional pediatric organizations worldwide, issued guidance for judicious screen time by children in particular. Digital media was discouraged for toddlers younger than 24 months of age other than for video chatting and no more than 1 hour per day of high-quality programming was recommended for preschool children. Today, when screen time is a necessity rather than an option, these evidence-based guidelines have been set into a necessary rebalance. In fact, the American Academy of Child and Adolescent Psychiatry has emphasized the importance of the use of media to strengthen connections across homes and schools, alongside offline time and high-quality resources that are educational and age-appropriate.

The accelerated transition to online communication and work has profoundly changed the delivery of health care services, now relying on telemedicine not only to reach rural and remote communities as in the past, but for routine care in urban communities alike. In our ethical evaluation of this transition, we place issues of access in the foreground. Both for those who are historically underserved and those who are currently required or encouraged to limit physical contact outside the home, tele-care is clearly better than no care. Telemedicine has its challenges though: the physical examination is limited to words without touch, and evaluations of behavioral health and family dynamics are limited by the availability and capabilities that technology affords to participants who seek to engage [11,12]. Still, for conditions involving mental health, remote assessment has been shown to be effective; for movement disorders requiring detailed neurological examination, less so. Best practices to ensure not only the effectiveness of telemedicine, but also social justice around its use, have yet to be developed.

Online communication for professional and social activity has also been enabled by various online platforms such as Zoom, Microsoft Teams, and Facetime. While mitigating the adverse effects of social isolation and fractured togetherness with coworkers, much remains to be understood about the impact of continuous screen time for these purposes, for example, on cognitive and executive functions such as attention, decision-making, and speed of information processing. Digital media has immense value because of its ability to connect people while allowing physical separation. Managing the potential harms of online excess, however, is a key challenge.

Concluding Remarks and Future Perspectives

COVID-19 continues to challenge society economically, socially, and ethically, including through still unfolding effects on the brain and mental health. The pandemic has brought to the foreground debates on timely access and rights to health services. As in many of the 21st century viral epidemics, health disparities have been magnified, particularly in relation to marginalized, rural, and remote communities where comorbidities are prevalent [13,14]. A spectrum of mental health challenges manifest during the course of a viral epidemic; front line workers are not alone in feeling the impact, but the anticipation they face for the care they must provide is a special case for concern. Efforts to establish empirical and authoritative guidance for screen time to ensure safe use, especially among youth, have been trumped. Moreover, even as countries gain a grasp on the near-term impact of COVID-19 on economic recovery, balancing economic reopening with viral suppression efforts when the long-term sequelae, including neurological ones, are very much unknown, is a delicate endeavor. These and many other knowledge gaps require further neuroscience, neuroethics, epidemiologic, social, and cognitive studies (see Outstanding Questions). We hope that this opinion piece offers a useful starting point in the conversation on issues at the intersection of COVID-19 and society that merit that the broadest range of neuroethical attention.

Outstanding Questions

What are the ethical responsibilities of the neuroscience community to pursue research on neurological sequelae of COVID-19? Where should priorities lie?

How can the ethics, public health, social, and legal research of neuroethicists be situated to most closely align with and contribute impactfully to the neuroscience of COVID-19?

What will be the long-term impact of anticipatory stress on the mental well-being of health care workers at the front lines of the COVID-19 pandemic?

What would be an adequate balance between the need for remote connectivity and managing screen time to preserve and promote brain health across different age groups during the pandemic?

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