



**Update on Mental Health Aspects of  
SARS-CoV-2 Pandemic:  
How Trauma Affects Mental Health of  
Individuals and Populations**

August 3, 2021

# Main Points

- **Traumatic life events affect individuals differently.**
- **A substantial minority of people (over 1/3) who are exposed to a localized disaster will develop a variety of clinically significant symptoms of anxiety, depression, substance use, insomnia and post traumatic stress.**
- **The effects of SARS-CoV-2 on US general population's depression, anxiety, substance use and stress associated symptom measures are consistent with population responses to localized disasters.**
- **People with pre-existing mental health disorders are more susceptible to the effects of stressful life events, this pattern was confirmed by multiple studies worldwide during SARS-CoV-2.**
- **Traumatic life events are the single largest determinant of anxiety and depression symptoms and combine with the person's thinking style to augment or minimize those symptoms.**

## Main Points (2)

- **Health care workers with direct contact with the infected during a pandemic have the highest risk for psychological distress.**
- **Previous pandemic survivors of MERS and SARS-COV-1 report significant persistent mental health effects at one year post infection.**
- **SARS-CoV-2 acute infection can impact the survivors' mental health in the short term (14 to 90 days after acute treatment); the most frequently reported effect was reoccurrence of a previous mental health disorder.**
- **Structural brain changes (loss of gray matter) and brain metabolic changes have been observed six months after acute SARS-CoV-2 infection.**
- **The physiological mechanism of the SARS-CoV-2 post infection neurological effects is unknown, but researchers have proposed a mechanism of virus infection of capillary endothelium and a resulting inflammatory cascade.**

# Principle #1: Traumatic Events Affect Individuals Differently and Can Induce Different Responses in People Who Experienced the Same Traumatic Event

- **Trauma is a risk factor for virtually all mental disorders (particularly depressive, anxiety, dissociative and personality disorders),**
- **Some trauma survivors are resilient, some develop PTSD and others develop other mental disorders,**
- The variety of symptoms that trauma survivors express (mood, cognitive, perceptual, somatic), make it difficult to classify.
- **Traumatic stress defies categories, the authors conclude that Post Traumatic Stress is currently best conceptualized as a specifier for other mental disorders.**

Guina, Baker, Stinson, Maust, Coles, Broderick, 2017

# Mental Health Aspects of Fort McMurray Wildfire

- The 2016 wildfires in Fort McMurray (Alberta, Canada) led to displacement of 88,000 people.
- Estimate the prevalence of post-traumatic stress, major depressive, insomnia, generalized anxiety, and substance use disorders in the adult population of Fort McMurray 1 year after.
- Methods: A phone survey of 1500 evacuees.
- Results: **38% had a probable diagnosis of either post-traumatic stress, major depressive, insomnia, generalized anxiety, or substance use disorder, or a combination of these.**
- Insomnia disorder was the most common, with an estimated prevalence of 28.5%.
- **Post-traumatic stress, major depressive and generalized anxiety disorders were almost equally prevalent, with ~15% each.**
- The estimated prevalence of substance use disorder was 7.9%.
- Conclusion: **One year after the fires, more than one third of the evacuees had clinically significant psychological symptoms** (Belleville, Ouellet, Lebel et al., 2021).

# SARS-CoV-2 Population Mental Health Effects

- Assess mental health and substance use during the pandemic, representative panel surveys among adults aged  $\geq 18$  years across the US during June, 2020.
- **Overall, 40.9% of respondents reported at least one adverse mental or behavioral health condition,**
- Symptoms of anxiety disorder (25.5%) or depressive disorder (27.8%), trauma and stressor-related disorder related to the pandemic (26.3%), and
- Started or increased substance use to cope with stress or emotions related to SARS-CoV-2 (13.3%) Czeisler, Lane, Petrosky et al., 2020).
- **The mental health symptoms reported and their frequency are consistent with a response to a local disaster.**

## Principle #2: Pre-Existing Mental Health Disorders Sensitize People to the Effects of Traumatic Events

- **Disasters:** Most of the extensive literature over the past 30 years suggests that disasters have psychopathological consequences as well as medical and social ones.
- **Pre-existing disorders appear to be risk factors for further psychopathology after a disaster** (Katz, Pellegrino, Pandya, Ng, DeLisi, 2012; Bromet, Atwoli, Kawakami et al., 2017; Lowe, Raker, Waters, Rhodes, 2020).
- **Individual traumatic events: The psychiatric condition prior to the accident could be identified as a predictor for the development of Axis I disorders.**

## Mental Health Aspects of Fort McMurray Wildfire: Risk Factors

- Objective (2): To identify disaster correlates of mental health disorders.
- Results: **For all five mental health disorders, having a mental health condition prior to the fires was a significant risk factor, as well as having experienced financial stress or strain due to the economic decline already present in Fort McMurray.**
- **Five post-disaster consequences were significant predictors of four of the five disorders: decrease in work, decrease in social life,** poorer current health status, increase in drug and alcohol use, and higher level of stress experienced since the fires.
- **Conclusion: This study helped identify individuals more at risk for mental health issues after a natural disaster and could guide post-disaster psychosocial support strategies** (Belleville, Ouellet, Lebel et al., 2021).



# SARS-CoV-2 Studies Found Pre-existing Mental Health Disorders a Risk Factor for Increased Levels of Distress

- Multiple studies across the world found pre-existing mental health disorders as a risk factor for developing a new mental health disorder or more severe mental health symptoms during SARS-CoV-2.
- **Worldwide Internet Survey:** Plomecka, Gobbi, Neckels et al., 2021
- **France:** Megalaki, Kokou-Kpolou, Vaudé et al., 2021
- **Italy:** Fiorillo, Sampogna, Giallonardo et al., 2021; Castellini, Rossi, Cassioli, 2021; Tarsitani, Vassalini, Koukopoulos et al., 2021.
- **India:** Hazarika, Das, Singh, Bhandari, Sharma, 2021.
- **China:** Ting, Wong, Liu et al., 2021.
- **USA and Canada:** Asmundson, Paluszek, Landry et al., 2020.



**A Mixed Variety of Symptoms of Anxiety, Depression, Substance Use, Insomnia and Post Traumatic Stress are a Common Disaster Response.**

**Assessing Depressive Symptoms in Isolation Can Be Misleading.**

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# SARS-CoV-2 COVID

## US General Population Depression Effects

- **To estimate the prevalence of depression symptoms among US adults during versus before the SARS-CoV-2 pandemic.**
- Used 2 population-based surveys of US adults aged 18 or older.
- During SARS-CoV-2, estimates were derived from the Life Stressors Impact on Mental Health and Well-being study, conducted from March 31 to April 13, 2020.
- Before SARS-CoV-2 estimates were derived from the National Health and Nutrition Examination Survey, conducted from 2017 to 2018.
- Main outcomes: Depression symptoms, defined using the PHQ-9 cutoff of 10 or higher. Categories of depression symptoms were defined as none (score, 0-4), mild (score, 5-9), moderate (score, 10-14), moderately severe (score, 15-19), and severe (score,  $\geq 20$ ).

## SARS-CoV-2 US General Population Depression Effects (2)

- Depression symptom prevalence was higher in every category during SARS-CoV-2 compared with before SARS-CoV-2.
- Higher risk of depression symptoms during SARS-CoV-2 was associated with having **lower income, having less than \$5000 in savings**, and exposure to more stressors.
- **Individuals with lower social resources, lower economic resources, and greater exposure to stressors (e.g., job loss) reported a greater burden of depression symptoms** (Ettman, Abdalla, Cohen et al., 2020).
- **It is unclear whether this study assesses general pandemic distress versus clinically significant major depression. As with other disaster studies, people with limited financial resources or who experience financial effects from the disaster are likely to have more severe mental health responses.**

## Principle #3: Traumatic Life Events Are the Single Largest Determinant of Anxiety and Depression Symptoms

- Researchers analyzed the responses of over 32,000 participants, aged 18 to 85 years, who completed the BBC's 'Stress Test', an online survey to explore the causes and consequences of stress.
- The study, the biggest of its kind in the UK, found **that traumatic life events were the single biggest determinant of anxiety and depression** followed by a family history of mental illness and income and education levels.
- Relationship status and social factors made smaller, but still significant contributions to stress.
- However, the **results revealed that a person's thinking style was as much a factor in the level of anxiety and depression a person experienced.**

Kinderman, Schwannauer, Pontin, Tai, 2013; Kinderman, Tai, Pontin, Schwannauer, Jarman, Lisboa, 2015

# Treatment of Mild to Moderate Depressive Symptoms Associated with Traumatic Life Events

- **Psychotherapy is the recommended treatment for mild to moderate depression** (Fournier, DeRubeis, Hollon et al., 2010; Cuijpers, Andersson, Donker, van Straten, 2011; Amick, Gartlehner, Gaynes et al., 2015; Furukawa, Weitz, Tanaka et al., 2017; Gartlehner, Wagner, Matyas et al., 2017).
- Psychotherapy can be especially effective when depressive symptoms are a response to a traumatic life event, because the event and associated thoughts are more consciously accessible.
- The pandemic has normalized telehealth and especially telehealth mental health visits, patients experiencing mild to moderate depressive and anxiety symptoms with onset during SARS-CoV-2 should be encouraged to use telehealth mental health services.

# Is the Cure Really Worse Than the Disease?

## The Health Impacts of Lockdowns During SARS-CoV-2

- Restrictive interventions against SARS-CoV-2 (known as ‘lockdowns’) are associated with health harms.
- **However, it is challenging to determine whether lockdowns have caused the harms or whether these harms are a direct consequence of the underlying health disaster of the pandemic.**
- Careful analysis of excess mortality suggests that lockdowns are not associated with large numbers of deaths in places that avoided large SARS-CoV-2 epidemics (eg, Australia, New Zealand).
- This evidence must be weighed against the very severe harms caused by SARS-CoV-2 itself, as seen for example in Brazil and India.
- **It is unlikely that government interventions have been worse than the pandemic itself in most situations using data collected to date.**



# **Health Care Workers (HCW), Who Directly Care for Pandemic Patients Are at the Highest Risk for Psychological Distress**

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# HCW Pandemic Mental Health Review

- The 24 studies included in this review reported data predominantly from China (18 out of 24 included studies).
- Most sampled urban hospital staff.
- **Our study indicates that SARS-CoV-2 has a considerable impact on the psychological wellbeing of front-line hospital staff.**
- **Results suggest that nurses may be at higher risk of adverse mental health outcomes during this pandemic.**
- No studies compared nurses with the **primary care workforce.**
- Furthermore, no studies investigated the psychological impact of the SARS-CoV-2 pandemic on **social care staff.**

# Health Care Workers Who Have Direct Contact with Affected Patients Have the Highest Risk of Mental Health Effects

- 59 papers met the inclusion criteria: 37 were of severe acute respiratory syndrome (SARS), eight of SARS-CoV-2, seven of Middle East respiratory syndrome (MERS), three each of Ebola virus disease and influenza A virus subtype H1N1, and one of influenza A virus subtype, H7N9.
- Compared with lower risk controls, **staff in contact with affected patients had greater levels of both acute or post-traumatic stress (odds ratio 1.71, 95% confidence interval 1.28 to 2.29) and psychological distress (1.74, 1.50 to 2.03).**

Kisely, Warren, McMahon, Dalais, Henry, Siskind 2020

# Pandemic Effects on HCW Mental Health

- There is very limited data on the effects of pandemics on HCW mental health.
- Data is lacking or very limited for some groups of HCW, such as, primary care and social work.
- The majority of HCW studies have assessed limited mental health symptoms, such as, post traumatic stress, anxiety or depression in isolation.
- There is very limited data on HCW substance use during and after pandemics.
- Much better data is needed to develop HCW support systems for both future pandemics and local disasters.



**SARS-CoV-2 Survivors Experience Similar Stress as the General Population Plus the Stress of a Potentially Fatal Disease and in Many Cases, Hospitalization.**

**In Addition, the Physiological Effects of SARS-CoV-2 Infection May Facilitate Neurological and Mental Health Disorders.**

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# 2003 SARS Pandemic Survivors

- 117 SARS survivors from Toronto, Canada, **approximately 50% of survivors diagnosed with a mental health disorder and in treatment one year after exposure** (Tansey, Louie, Loeb et. al., 2007).
- Taiwan: 285 SARS survivors at 12-year follow-up had an **increased risk of anxiety, depression, sleep disorders, posttraumatic stress disorder, acute stress disorder and suicide** (Tzeng, Chung, Chang et. al., 2020).
- Limitation: Only 5% of SARS survivors were followed and assessed at sites distant from the epicenter of the pandemic.
- The SARS epidemic provides limited evidence for significant mental health effects at 1 year post infection and long lasting effects up to 12 years later.

# MERS-COVID Survivors

- A study conducted in Korea 12 months after the localized MERS outbreak assessed the one year mental health outcomes for 69 survivors of MERS.
- Results: **42.9% of survivors reported PTSD and 27.0% reported depression at 12 months post-MERS** (Park, Park, Lee et al., 2020).
- This is a stronger study in design and participation rates with 47% of the survivors assessed at one year.
- This study provides preliminary evidence of mental health effects of MERS in the majority of survivors one year post infection.

# Meta-analysis: SARS, MERS and SARS-CoV-2 Survivors

- Assess the psychiatric and neuropsychiatric presentations of SARS, MERS, and SARS-CoV-2.
- 65 peer-reviewed studies and seven preprints.
- The meta-analysis indicated that in the post-illness stage the point prevalence of **post-traumatic stress disorder was 32.2%**; 121 of 402 cases from four studies), that of **depression was 14.9%**; 77 of 517 cases from five studies), and that of **anxiety disorders was 14.8%**; 42 of 284 cases from three studies).
- **Clinicians should be aware of the possibility of depression, anxiety, fatigue, post-traumatic stress disorder, and rarer neuropsychiatric syndromes in the longer term.**

# Mental Health Sequela of US SARS-CoV-2 Survivors

- Background: we assessed whether a diagnosis of SARS-CoV-2 (compared with other health events) was associated with increased rates of subsequent psychiatric diagnoses.
- Methods: used the TriNetX Analytics Network, a global federated network that captures anonymized data from electronic health records in 54 health-care organizations in the USA, totaling **69.8 million patients**.
- TriNetX included **62,354 patients** diagnosed with SARS-CoV-2 between Jan 20, and Aug 1, 2020.
- Measured the incidence of and hazard ratios (HRs) for psychiatric disorders, dementia, and insomnia, during the first 14 to 90 days after a diagnosis of SARS-CoV-2.

Taquet, Luciano, Geddes & Harrison, 2020



# Mental Health Sequela of US SARS-CoV-2 Survivors (2)

- A diagnosis of SARS-CoV-2 was associated with **increased incidence of a first psychiatric diagnosis** in the following 14 to 90 days compared with six other health events (influenza; other respiratory tract infections; skin infection; cholelithiasis; urolithiasis, and fracture of a large bone; all  $p < 0.0001$ ).
- The risk was greatest for **anxiety disorders, insomnia, and dementia**.
- **The incidence of any psychiatric diagnosis in the 14 to 90 days after COVID-19 diagnosis was 18.1% (95% CI 17.6–18.6), including 5.8% (5.2–6.4) that were a first diagnosis.**
- **The incidence of a first diagnosis of dementia in the 14 to 90 days after COVID-19 diagnosis was 1.6% (95% CI 1.2–2.1) in people older than 65 years.**
- **Interpretation: Survivors of SARS-CoV-2 appear to be at increased risk of psychiatric sequelae.**

Taquet, Luciano, Geddes & Harrison, 2020

# Mental Health Sequela of Pandemics

- Heightened stress responses are likely to manifest in three ways:
- **1) A new episode of a disorder in those with a predisposition to a major psychiatric disorder or an acute exacerbation in those who already have such a disorder,**
- **2) A trauma or stressor related disorder, such as acute stress disorder, PTSD, or adjustment disorders, and**
- **3) A symptomatic stress response that does not meet the diagnostic criteria of a psychiatric disorder.**
- Numerous psychological effects follow pandemics: **alcohol use, PTSD, anxiety, anger, fear of contagion, perceived risk, uncertainty, and distrust** are a few of the immediate and long-term effects that are likely to result from the SARS-CoV-2.

## Mental Health Sequela of US SARS-CoV-2 Survivors (4)

- **The most troubling aspect of this study is the 1.6% new onset dementia in the survivors aged 65 and older at 14 to 90 days post infection survival.**
- One of the only comparable exposures that results in dementia within an one year time frame among people aged 60 and over is acute ischemic stroke.
- In a study of 927 patients with acute ischemic stroke in the Stroke Data Bank cohort, the probability of new-onset dementia at 1 year was 5.4% for patients aged 60 years and over.

Tatemichi, Foulkes, Mohr, Hewitt, Hier, Price and Wolf 1990

# SARS-CoV-2 Neurological Effects

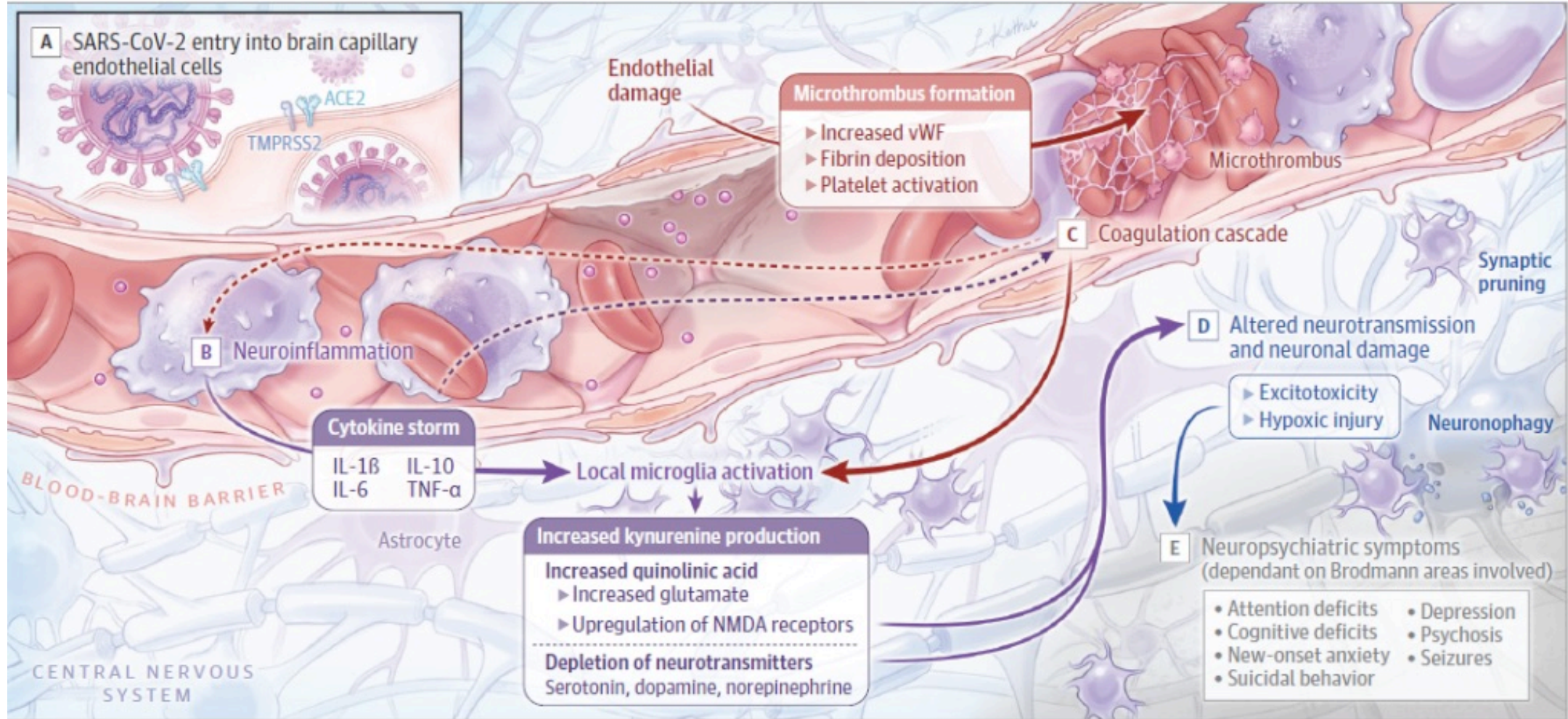
- MERS-CoV and SARS-CoV have been associated with neurological disease in rare cases.
- **SARS-CoV-2 infection is associated with a wide spectrum of neurological syndromes affecting the whole nervous system, including the cerebral vasculature** (Paterson, Brown, Benjamin et al., 2020).
- **Short and long-term neuropsychiatric symptoms (NPS) and long-term brain sequelae often accompany the respiratory and gastrointestinal symptoms of SARS-CoV-2.**
- Some SARS-CoV-2 patients present with anosmia, cognitive and attention deficits (i.e. brain fog), new-onset anxiety, depression, psychosis, seizures, and suicidal behavior.
- The NPS present before, during, and after respiratory symptoms and are unrelated to respiratory insufficiency, **suggesting independent brain damage.**
- Follow-ups conducted in Germany and the United Kingdom found post-SARS-CoV-2 NPS in 20% to 70% of patients, even in young adults, and lasting months after respiratory symptoms resolved, **suggesting brain involvement persists.**

## SARS-CoV-2 Neurological Effects (2)

- SARS-CoV-2 is known to penetrate the olfactory mucosa, causing loss of smell, and may enter the brain, migrating from the cribriform plate along the olfactory tract or through vagal or trigeminal pathways; however, definitive evidence for this is lacking.
- Entering through angiotensin-converting enzyme 2 receptors, SARS-CoV-2 can damage endothelial cells leading to inflammation, thrombi, and brain damage (Meinhardt, Radke, Dittmayer et al., 2021).
- Systemic inflammation leads to decreased monoamines and trophic factors and activation of microglia, resulting in increased glutamate and *N*-methyl-D-aspartate (NMDA) and excitotoxicity (Roman & Irwin, 2020).
- These insults induce new onset or re-exacerbation of preexisting NPS.



# Brain Vascular Injury, Neurotransmitter System Dysfunction, Thrombotic Events, Neuronal Damage, and Neuropsychiatric Symptoms



# SARS-CoV-2 Effects on Brain Structure

- Data from 782 participants from the UK Biobank SARS-CoV-2 re-imaging study.
- 394 participants tested positive for SARS-CoV-2 infection between their two scans.
- Objective: to compare longitudinal brain changes between these 394 COVID-19 patients and 388 controls who were matched for age, sex, ethnicity and interval between scans.
- Identified **significant effects of SARS-CoV-2 in the brain with a loss of grey matter** in the left parahippocampal gyrus, the left lateral orbitofrontal cortex and the left insula.
- **Our findings thus consistently relate to loss of grey matter in limbic cortical areas directly linked to the primary olfactory and gustatory system.**

# SARS-CoV-2 Effects on Brain Metabolism

- Objective: describe longitudinal brain metabolism of SARS-CoV-2 related encephalopathy.
- Methods: seven patients with variable clinical presentations of SARS-CoV-2 related encephalopathy were explored thrice with brain 18F-FDG-PET/CT, once in the acute phase, 1 month later and 6 months after COVID-19 onset in comparison with 32 healthy controls.
- Results: neurological manifestations during acute encephalopathy were heterogeneous. However, all presented with predominant cognitive and behavioral frontal disorders. SARS-CoV-2 RT-PCR in the CSF was negative for all patients. MRI revealed no specific abnormalities for most of the subjects. All had a **consistent pattern of hypometabolism in a widespread cerebral network including the frontal cortex, anterior cingulate, insula and caudate nucleus.**



## SARS-CoV-2 Effects on Brain Metabolism (2)

- Six months after onset, the majority of patients clinically had improved but **cognitive and emotional disorders of varying severity remained with attention/executive disabilities and anxiety and depressive symptoms, and lasting prefrontal, insular and subcortical 18F-FDG-PET/CT abnormalities.**
- Conclusion: this study suggests that this network remains mildly to severely impaired 6 months after SARS-CoV-2 disease onset.

Kas, Soret, Pyatigorskaya et al., 2021

# Main Points

- **Traumatic life events affect individuals differently.**
- **A substantial minority of people (over 1/3) who are exposed to a localized disaster will develop a variety of clinically significant symptoms of anxiety, depression, substance use, insomnia and post traumatic stress.**
- **The effects of SARS-CoV-2 on US general population's depression, anxiety, substance use and stress associated symptom measures are consistent with population responses to localized disasters.**
- **People with pre-existing mental health disorders are more susceptible to the effects of stressful life events, this pattern was confirmed by multiple studies worldwide during SARS-CoV-2.**
- **Traumatic life events are the single largest determinant of anxiety and depression symptoms and combine with the person's thinking style to augment or minimize those symptoms.**

## Main Points (2)

- **Health care workers with direct contact with the infected during a pandemic have the highest risk for psychological distress.**
- **COVID virus pandemic survivors are at high risk for adverse effects on their mental health.**
- **SARS-CoV-2 acute infection can impact the survivors' mental health in the short term (14 to 90 days after acute treatment) ); the most frequently reported effect was reoccurrence of a previous mental health disorder.**
- **Structural brain changes (loss of gray matter) and brain metabolic changes have been observed six months after acute SARS-CoV-2 infection.**
- **The physiological mechanism of the SARS-CoV-2 post infection neurological effects is unknown, but researchers have proposed a mechanism of virus infection of capillary endothelium and a resulting inflammatory cascade.**

# Thank You

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# Appendix

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# The Evidence Base for the Use of Psychotherapy For Mild to Moderate Depression

- **Meta analytic evidence supports that psychotherapy is equivalent to antidepressant treatment for mild to moderate depressive symptoms** (PHQ-9 scores 5 to 14) and is also effective for severe depressive symptoms (Cuijpers, Andersson, Donker, van Straten, 2011).
- Multiple more recent meta analytic studies replicated the findings of **similar effectiveness of CBT to second generation antidepressants across the range of depression severity** (Amick, Gartlehner, Gaynes et al., 2015; Furukawa, Weitz, Tanaka et al., 2017; Gartlehner, Wagner, Matyas et al., 2017).
- A meta analysis found that **antidepressants demonstrated clinical benefit over placebo only at PHQ-9 scores of 20 and above** (Fournier, DeRubeis, Hollon et al., 2010).