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In the Know

A RAS and Bradykinin-Mediated Mechanism for COVID-19

Richard Simoneaux

Steven L. Shafer, MD
Editor-in-Chief

Since the initial outbreak of SARS-CoV-2 in Hubei province, China, in late 2019, infected individuals have displayed a number of different and seemingly unrelated clinical presentations, which has led to much confusion regarding the mechanism(s) by which SARS-CoV-2 affects human hosts.

SARS-CoV-2 gains entry to cells through attachment to angiotensin converting enzyme 2 (ACE2), one of the many peptides that comprise the renin-

angiotensin system (RAS), which plays a key role in regulating blood pressure, electrolytes, and intravascular volume.

Since SARS-CoV-2 directly targets the ACE2 surface-bound enzyme, scientists have attempted to explain the protean symptoms of COVID-19 in terms of dysregulation of the RAS. Garvin and colleagues intended to provide further detail into dysregulation of the RAS by RNA sequencing of nine bronchoalveolar lavage samples from patients with

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Psychological Distress of COVID-19: Are You at Risk?

Adam Roth, PhD

As we experience the collective trauma of COVID-19, medical professionals remain one of the most impacted groups. The exposure to stressors, either directly or witnessed, in which one feels overwhelmed by and helpless to risk and harm is prevalent. In their range of responsibilities, medical professionals directly experience or

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Perspectives: Is Anesthesia a Human Right?

Dibash Kumar Das, PhD

The Universal Declaration of Human Rights by the United Nations General Assembly declared that all human beings are entitled to certain universal, inalienable, indivisible rights, including access to adequate health care, regardless of their socioeconomic status or location (asamonitor.pub/2YWFntT; asamonitor.pub/31Pk9jE). The right to health implies access to all care, including anesthesia. Yet, there is an urgent need to address large gaps in anesthesia services globally. Examples of the anesthesia care gap include:

- Of the world's 7.8 billion people, 5 billion are without access to safe and affordable surgical care when needed (asamonitor.pub/2EQU1fc). Access is

worst in low-income and middle-income countries, where as much as 90% of the population cannot access basic surgical care.

- Out of the 313 million surgical procedures performed globally each year, only 6% occur in low-income and middle-income countries, where over one-third of the world's population lives (asamonitor.pub/2EQU1fc).
- A significant proportion of the global population has limited access to opioid analgesics for pain relief. 250 million (4%) have moderate access, 460 million (7%) have adequate access, and insufficient data are available for 430 million people (7%) (*J Pain Palliat Care Pharmacother* 2011;25:6-18).

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SPECIAL SECTION

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witness highly stressful and traumatic events related to COVID-19, such as personal exposure or risk of exposure, risk of exposing others, and witnessing the pain/suffering and death of patients. The vulnerability and susceptibility to stress and trauma is escalated when one has the experience of being under-supported, under-resourced, under-equipped, under-protected, undervalued, and under-acknowledged.

Examples of the distress on the front lines of COVID-19 are prevalent. In interviews from the *New York Times* and National Public Radio (April 14, 2020, May 5, 2020), for example, emergency physicians describe their experiences:

- “This virus is more infectious than anything we’ve ever seen before. When influenza waves are going through the hospital, everyone is not – we’re not – influenza never – and you always got a vaccine. The infection rate from influenza is nothing compared to this... and I’m scared every day. I’ve never been scared as a doctor before.... All the structures that we trust – I mean, whether it’s government or health systems or the preventive apparatus of the world – has been shown to be so flawed.”
- “We’re almost observers in this. We can put patients on oxygen. We can intubate them in the ICU. But we’re mainly trying to allow the body to heal on its own. Dealing with COVID largely means dealing with a feeling of helplessness.”
- “When I put all the PPE on and I’m ready to enter the room and I open that door, the very first thought that goes through my mind is not the patient’s well-being. It’s, ‘did I put the PPE on correctly?’... That is an awful feeling.”

Signs of distress

Psychological distress following exposure to a traumatic or stressful event is quite variable (*American Psychiatric Association* 2013). Symptoms beginning immediately and up to one month after a trauma are associated with the diagnosis of Acute Stress Disorder. Symptoms persisting beyond or having onset after one month from a trauma are associated with the diagnosis of Post-traumatic Stress Disorder. Symptoms of psychological distress are adaptations or adjustments one makes to psychologically manage, rebalance, or survive a traumatic event. Symptoms may not be at a clinical level, yet are an indicator of functioning becoming limited and one’s need for attention and care.

The DSM 5 identifies four characteristic phenotypes of symptoms of distress following aversive or catastrophic events:

1. *Anxiety or fear-based emotional reactions*: Experiencing excessive nervousness, worry, distress, anxiety, or fears. Re-experiencing events through night-



mares, flashbacks, or intrusive thoughts and emotions. Distress triggered by external reminders or by intrusive memories. Avoidance of memories and external reminders.

2. *Arousal and reactive-externalizing*: Irritable, angry and aggressive emotions, and related behaviors. Outbursts, yelling, arguing, getting into fights. Risk-taking, destructive, and addictive behaviors. Heightened sensitivity, both emotionally and to potential threats. Hypervigilance, heightened startle response, jumpiness.
3. *Anhedonic and dysphoric mood with negative cognitions*: Low or depressed mood, lack of interest or participation in activity, isolation, lack of positive emotions and excitement, flattened or blunted affect, low energy, and fatigue. Persistent and exaggerated negative beliefs or expectations about oneself or others, or the world. Thoughts and emotions of anger, sadness, blame, guilt, shame, confusion.
4. *Dissociative experiences of unreality or detachment*: Experiences of depersonalization – experiencing an unfamiliar-distorted-absent sense of self. Experiencing detachment, seeing oneself as an outside observer, of one’s thoughts, feelings, sensations, body, or actions. Experiencing perceptual alterations, distorted sense of time, emotional, or physical numbing. Experiences of derealization. Experiencing detachment, unfamiliarity or unreal perceptions with others or one’s surroundings. Dreamlike, foggy, lifeless, or visually distorted perceptions.

Additional and overlapping characteristics may include somatic symptoms such as elevated heart rate, shortness of or rapid breath, feeling hot or cold, tingling or numb sensation. Cognitive symptoms such as lack of concentration, focus, memory, disorganization, and uncertainty may emerge. Sleep disturbances such as difficulty falling asleep, interrupted, or restless sleep also may be experienced (*American Psychiatric Association* 2013).

Self-care and accessing support

After experiencing stressors or trauma, returning to a sense of balance and empowerment in one’s life begins with overcoming the feelings of helplessness and regaining safety and trust in ourselves, others, and the environment. The experience of adverse stress and trauma can have a significant and lasting impact that can be greatly reduced with care, support, and treatment. It is likely at times one will have to make conscious efforts to overcome avoidance or lack of energy to engage in self care and reaching out to others. This complication toward accessing support is associated with the tendency to be reluctant toward engaging in thoughts, emotions, and conversations related to a trauma. Create a plan, routine, structure, or schedule for your support and care. Fit it in when and where you can. The longer you hesitate or put it off, the greater the patterns of avoidance you will have to overcome (www.helpguide.org, www.ptsd.va.gov).

Presence and mindfulness

Present-centered mindfulness strategies are tools to get one out of the stressful past and grounded in the present. They keep you aware and focused in the here and now. With presence and mindfulness, one is less vulnerable to intrusive and overwhelming thoughts and emotions triggered by continuous and past stressful and traumatic events. Attention and awareness toward one’s own embodied experience can ground one in the present moment. Awareness of times when distress increases or is reduced can be both preventative and supportive. Examples are transition times to and from the work environment, recurrent distressing work events, leaving from and arriving into your home, and times when one makes efforts to relieve stress (www.helpguide.org, www.ptsd.va.gov).

Reduce stress levels

Without reduction and release, stressors accumulate, stress levels climb, and the frequency and intensity of distress increases. Use methods to empty your vessel of stress with a mix of both active and passive strat-



Adam Roth, PhD

Psychologist in private practice, Beachwood, Ohio.

egies. Achieve relaxation with calming and soothing activity. Release stress with active outlets. Use clearing, cleansing, and intentionality to process and relieve the difficulties of the day. Reflect on and release your experiences and emotions with creative expression. Reconnect from the detachment and dissolution with spiritual practice.

Take action

The following is a list of activities for relaxation, mindfulness, and stress relief. Engaging in restorative activities, especially after experiencing highly stressful or traumatic events, supports recovery and resilience. Preventative self care includes physical activity, eating a healthy diet, getting enough rest, making time for relaxation, and avoiding drugs and alcohol.

- Release bracing and intensity with movement and exercise: take walks, do cardio workouts, lift weights.
- Sooth yourself by taking a relaxing and cleansing bath, sitting quietly with a hot cup of tea; read, calm your mind with meditation.
- Get creative with music, art, writing, or cooking. Singing or vocal toning can rebalance the nervous system in times of distress.
- Connect with your spiritual resources, spiritual or religious practices, prayer, or spend time outdoors in nature.
- Combine mind, body, and spirit with practices such as dance, yoga, or Tai Chi. Clean and organize your home or office.
- Spend time clearing your space of clutter and getting rid of things you don’t need.

Seek support

Access your social support network by reaching out to friends, family, colleagues, and clergy. Debrief work experiences with a colleague. It can be very helpful to confide in friends and family, share your stories, or just have fun together to escape the stressors. One-sided interactions can be draining and dissatisfying, so create mutuality in the relationships of support, and work together to feel better.

When distress is high and without much relief, seek out clinical support and treatment. Seek effective psychotherapy and counseling with techniques such as exposure therapy, hypnotherapy, biofeedback, somatic psychotherapy, and cognitive behavioral therapy. Consider a visit with a prescriber; medication can be effective for severe and persistent symptoms. ■