

A Perfect Storm

By Yasmin L. Hurd, Ph.D., and Timothy Brennan, M.D.

Our authors, who direct the Addiction Institute for the Mount Sinai Health System in New York City, address the substance-abuse avalanche brought on by the Covid-19 pandemic.

AS AMERICAN ADDICTION RESEARCHERS AND TREATMENT PROFESSIONALS WENT TO SLEEP ON NEW YEAR'S EVE 2019, they were likely feeling pretty optimistic. Overdose death [rates](#) involving heroin, while still high, had dropped for the third year in a row. Indeed, it seemed like the opioid crisis had not only plateaued but was slowly starting to improve. Access to medication-assisted treatment had increased around the country; and for the first time in history, a variety of [health tech startups](#) were looking to leverage their expertise in innovative ways to bring treatment to economically disadvantaged areas.

None of us knew that we would soon be facing an unprecedented storm. Indeed, it would be a perfect storm, particularly for vulnerable groups such as those suffering from substance-use disorders. On February 11, 2020, Covid-19 became the official name given by the World Health Organization for the highly infectious disease caused by infection with the SARS-CoV-2 coronavirus—and of a pandemic that would transform the world, creating a new norm of social distancing, isolation, and loneliness that exacerbated substance-use disorders.

The bedrock of modern addiction treatment is the fellowship gained by participating in group therapy, either in formal settings such as addiction treatment programs, or informal settings such as Alcoholics Anonymous (AA). When people first seek help for their addiction, they often feel impossibly alone and adrift. They can't conceive that anyone else in all of human history has ever felt the way that they feel. They are lonely, ashamed, and terrified. But when they start meeting other people with the same condition, something magical happens; they realize that not only are they not alone but there is a way through their suffering, a light at the end of the tunnel.

The group setting, which at the outset may have felt absolutely terrifying, will frequently become their refuge—a place where they can be fully present, fully accountable, and fully accepting of their disease. The oft-repeated mantra of “90 meetings in 90 days” exists for good, practical reasons: Active addiction takes up an extraordinary amount of time in people's lives; the relentless pursuit of acquiring, using, and recovering from the effects of a substance can crowd out almost all of their other responsibilities. People in early recovery suddenly have a lot of [time on their hands](#), and self-help and group therapy settings provide a safe place to spend it.

But as America entered the Covid lockdown in March of 2020, formal and informal addiction treatment settings were quickly forced to close down. A warm and welcoming AA meeting full of tears, laughter, and hugs, which previously might have felt like one of the safest places in the world, suddenly became one of the most unsafe. For people who had already established a network of recovery supports, the migration to online-only meetings was an annoyance, but not insurmountable. But for those who had not yet established themselves in recovery, an important lifeline now required a high-speed internet connection and involved the awkwardness of “meeting” people online when you have never met them in person.

Storm Clouds Form

Not surprisingly, the massive rise in unemployment, disruptions in work/life balance, and general stress and anxiety induced by the pandemic led to increased reliance on both healthy and unhealthy coping mechanisms. Just as sales of [exercise bikes](#) and yoga mats soared, so too did [alcohol consumption](#). Prior to the pandemic, it was both socially unacceptable and unprofessional to consume alcohol while working. But as people became accustomed to the “work from home” lifestyle, the social boundaries of office culture started to melt away. Who would know if a bottle of wine that would have been uncorked at 6 p.m., was now poured at 4 p.m.?

Not only did alcohol sales increase dramatically during the pandemic, but so too did illicit drug consumption: Americans reported using substances like alcohol and cannabis more than ever to cope with anxiety and stress. There were also reports that the [illicit drug supply chain](#) became disrupted, which may have increased drug adulteration. What had previously been a steady flow of pure heroin became an unsteady supply of heroin adulterated with highly potent synthetic opioids like fentanyl and its analogues, which are more than 50 times more potent than heroin, and 100 times more potent than morphine.

Now, fentanyl contamination was being regularly detected in various drugs, including counterfeit pain pills and sedatives, such psychostimulants as methamphetamine and cocaine, and even cannabis. As overdose data started to trickle in during 2020, it soon became clear that all of the gains that had been made from 2017 to 2019 had been lost. Shockingly, [overdose death rates](#) in the US skyrocketed [higher than they have ever been](#) at any time during the opioid crisis—with synthetic opioids accounting for more than 60 percent.

This historic rise in overdose deaths was, of course, multifactorial—besides the turn to addictive substances to cope with Covid-related stress, the disruption in access to drug treatment, and adulteration with toxic synthetic opioids, more people were using drugs in isolation. This meant limited opportunity for others to provide lifesaving help by administering naloxone (an opioid antagonist also known as Narcan) when overdose occurred.

As more data became available regarding Covid-19 risks, disparity, and outcomes, it was evident that substance-use disorders were a significant underlying medical condition associated with [high risk](#) for severe Covid-19 illness. Not only were individuals with substance use disorders (SUD) at [increased risk](#) of Covid-19, but they also experienced significantly worse outcomes than those without SUD. Knowing that they were at increased risk of bad outcomes from Covid-19 further heightened the already elevated anxiety of the addicted, causing more reactive substance use and more death. Overall, a perfect storm.

Stress: A Neurobiological Force

Though Covid-related stressors increased psycho-pathological states of fear, depression, and anxiety in most people, these were more elevated in individuals with SUD. Numerous factors associated with Covid—from social distancing and lockdown isolation to economic downturn—converge in the state of mental or emotional strain or pressure we call “stress.” [Biologically](#), stress refers to the body’s response to change. Clearly, the pandemic involved profound changes and demands in all aspects of life. This development was not unexpected: It is well documented that individuals at risk for addiction and those already suffering from it are particularly [sensitive to stress](#)—a reflection of the intricate links between the brain’s stress and reward systems.

[Addiction neurobiology is an extremely complex system](#) that involves numerous neurochemicals and interconnected circuits, all of which are influenced by both internal and external stressors. Each phase of addiction—intoxication, habitual compulsive drug-seeking, withdrawal, abstinence—can result in changes to our neurobiology. One of the most important chemicals in our brain’s “reward pathway” is the neurotransmitter dopamine. Most drugs of abuse will directly or indirectly increase dopamine in this pathway. Stress, especially acute or intense stress, boosts dopamine in these same brain areas, via the release of such compounds as corticotrophin-releasing hormone and cortisol. Consequently, stress can heighten reward sensitivity, potentiating the reinforcing effects of drugs. Conversely, drug use can sensitize the brain to stress.

In its attempt to protect the brain against the effects of acute stress, the body recruits neurobiological processes that feedback to increase neurochemicals that reduce dopamine levels and normalize other neurobiological systems (e.g., production of stress hormones). With repeated drug use or chronic stress, however, the biological picture changes: the brain is highly plastic and attempts to return neurobiological systems to “normal,” can lead to adverse pathological states.

For example, chronic use of drugs can result in reduced baseline dopamine release, decreasing the drug’s rewarding effects and increasing negative emotions. This phenomenon, “tolerance,” can have two effects: the user requires more and more of the drug to achieve the high experienced initially; and now he or she also needs the drug to provide relief of the negative mood state. The result: transition to uncontrolled compulsive drug use. By reducing dopamine levels, chronic stress also increases neurochemicals that promote stress, such as the neuropeptide called dynorphin, in brain areas such as the amygdala, which is involved in emotional regulation and drug-seeking behavior. Negative emotional states induced by these changes also drive compulsive drug-seeking behavior.

A vicious cycle is likely to occur. In trying to cope with stress, people begin to use drugs, thinking this will alleviate their negative mood. But during extended stressful periods, occasional self-medication readily escalates to regular use. This boosts output of stress-related hormones and neurotransmitters, contributing to heightened stress responsivity and negative emotional states, which in turn increase the motivation for continued drug use. Even individuals maintaining drug abstinence prior to Covid were at great risk for relapse during the pandemic, since withdrawal is dominated by negative affect and activation of the stress and anxiety systems that contribute to drug-craving.

The Vulnerable Brain

A particularly challenging dynamic of the pandemic has been the lack of in-person socialization for children and adolescents. The human brain has evolved to maximize social interaction and connectivity, which are dependent on the precise orchestration of complex neurodevelopmental processes. Forced isolation, lack of peer support, and minimal teacher oversight created a perfect storm for heightened stress and risky decision-making. Although restrictions have eased considerably with new variants, the support of peers and schools that is a central part of children’s daily lives, could disappear again. Friendships, cliques, sports, and extra-curricular activities may again be fundamentally altered. An entire social structure might once more be disrupted.

For many children, school is the only predictably safe and nurturing place in their lives. In the 2020 academic year, they were uprooted from this stabilizing force and required to attend school virtually. We know from developmental neurobiology that the [adolescent brain](#) is uniquely vulnerable to addiction due to a genetically programmed increase in risk-taking and anxiety-related behaviors driven by the amygdala, coupled with a relatively immature “executive” cognitive control center in the brain (the prefrontal cortex), which does not reach full maturity until the third decade of life. Differences in the development of executive versus emotional networks in the adolescent brain make adolescents more sensitive to rewarding and [stressful stimuli than adults](#). So, as challenging as Covid lockdown was for most adults, it was more difficult and neurobiologically perilous for most teens.

Significant neurodevelopment continues well into adolescence, as is evident in various brain structures. Particularly relevant to stress, social connectivity, and addiction is the profound functional and structural maturing of the amygdala, prefrontal cortex, and ventral striatum. For instance, activation of the ventral

striatum in response to reward (including social reward) is stronger in adolescents than in adults and children, which parallels the adolescent maturation of the dopamine system.

Adolescence is also a period of enhanced activity in the hypothalamic-pituitary-adrenal (HPA) axis—the neuroendocrine regulator of stress—and hormone levels following puberty enhance the stress response and increase the motivation and value of reward. Another critical maturation process during adolescence is in amygdala-[prefrontal cortex connectivity](#), a key neural circuit for the generation of negative affect and its regulation. The peak in social drive that occurs during adolescence coincides with this period of prefrontal cortex-amygdala maturation. Adolescence is a sensitive period of enhanced amygdala reactivity when emotional stimuli, stress, and social interactions are extremely important.

It should be emphasized that this period is also characterized by a relatively immature prefrontal cortex that is responsible for cognitive function. Indeed, cognitive control via inputs from the prefrontal cortex to the amygdala does not fully mature until early adulthood, leaving the ability of the prefrontal cortex to inhibit amygdala activity significantly low during adolescence. Stress further weakens this moderating process. Altogether, the neural signatures of adolescence parallel heightened reward sensitivity, stress sensitivity, and risk-taking as compared to other age groups. It's not surprising then that social environment or high-stress exposure at this time produces heightened vulnerability to anxiety-related disorders, a factor that is linked with a rise in [alcohol and drug use](#) associated with increased likelihood of addiction later in life.

Out of the Storm

While the emergence of new variants and uncertainty prolongs our fragile state, the pandemic has not been all doom and gloom. The Covid storm, like any crisis, has also provided opportunities—including a chance to develop new strategies to help individuals suffering from substance use disorders.

Perhaps one of the most unexpected outcomes of the pandemic has been the profound relaxation in regulatory laws that govern addiction treatment, particularly for the use of [buprenorphine](#), a medication for opioid-use disorder. Buprenorphine, like heroin or oxycodone, is an opioid, but it is nowhere near as euphorogenic or intoxicating. Substituting a very safe medication like buprenorphine for a very unsafe drug like heroin dramatically lowers the risk of overdose. Before the pandemic, it was very difficult to enroll someone onto buprenorphine over the phone or internet due to regulatory laws requiring in-person assessment for treatment. During the pandemic, virtual therapy became commonplace. Hard-to-reach areas that required a long drive for personal contact could now be accessed via an internet connection.

Another silver lining of the regulatory relief that occurred during the pandemic was the relaxation of laws regarding methadone maintenance treatment. Prior to Covid, many patients enrolled in methadone programs had to come to the clinic six days a week to pick up their dose. During Covid, they were able to stay safe in their homes and visit the clinic on a weekly or bi-weekly basis in order to pick up several doses at one time.

While it is still too early to judge the epidemiological impact of these liberalized policies, they have been very well-received by patients. In addition, accessing self-help groups like AA was [easier during the pandemic](#) for some people, as connecting through the phone or computer provided a protective layer of anonymity that overcame concerns about attending in person. Networks expanded, and new connections were made as people in New York City could suddenly join groups in Los Angeles or London. There is quite literally an AA meeting happening online [every hour of every day](#)—great news for those in recovery.

What remains to be seen is how long regulatory relief measures will stay in place. Will they become permanent, or will we backslide? As Americans return to the office and its associated etiquette, will alcohol consumption return to pre-pandemic levels, or has a new—and elevated—normal been created?

With new and perhaps future variants delaying any hope of an abrupt end to the pandemic, it remains critical that we leverage the insights that have been gained about disparities and vulnerable groups into new preventative and proactive measures. This is particularly true in regard to teenagers. Given the heightened stress reactivity of adolescence, and the possibility of long-lasting neural changes linked to Covid experiences, we must focus attention and support not only to help affected teens today, but to mitigate the development of addiction-linked psychopathologies in the future. Stay tuned.

Bios:

Yasmin Hurd, Ph.D., is a professor of psychiatry, neuroscience, and pharmacological sciences at the Icahn School of Medicine at Mount Sinai in New York City; director of the Addiction Institute at the Mount Sinai Behavioral Health System; Ward-Coleman Chair of Translational Neuroscience at Mount Sinai; and a member of the Dana Alliance for Brain Initiatives. She has conducted pioneering research on the neurobiology of opioid abuse, the neurodevelopmental (and crossgenerational) effects of cannabis, and potential treatments for opioid addiction. A member of the National Academy of Medicine, Hurd and her research have been featured on NPR, ABC, and CNN, and in the New York Times, Time, and Discover.

Timothy K. Brennan, M.D., is the chief of clinical services for the Addiction Institute of Mount Sinai in New York City and oversees addiction services across all campuses of the Mount Sinai Health System. He is also the director of the Fellowship in Addiction Medicine Program at the Icahn School of Medicine. Brennan completed his Fellowship in Addiction Medicine at The Addiction Institute, a Fellowship in Medical Ethics at Harvard Medical School, a residency in pediatrics at New York Presbyterian Hospital/Weill Cornell Medical College, and internship in Internal Medicine at Georgetown University Hospital.