Review

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The Mind Matters: How Stress and Mental Disruption Open the Door for COVID-19

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Abstract: **Background:** The emergence of the global coronavirus disease 2019 (COVID-19) pandemic brought with it unforeseen and unprecedented conditions for millions. Conspicuous disorders of the respiratory, gastrointestinal, and neurological systems have taken center stage, but an important category must be brought to the forefront: the psychological and emotional effects of this pandemic. Mandatory nationwide lockdowns, self-quarantining, and understandable anxiety about the unpredictable future are significant stressors and are having both detectable and undetectable impacts on mental and physical wellbeing. Negative affectivity including depression, loneliness, boredom, self-harm, and domestic violence doubled shortly after, as well as financial burden and unemployment. Mental health silently affects everyone and could be a deciding factor in recovery and remission of many health conditions and disorders. This paper assesses the impact of psychosocial stressors and the pandemic on the human body, focusing on the unseen effects of mental health that could be keeping the door open for COVID-19 and could have public health ramifications long after the pandemic is fully resolved. **Methods:** We conducted a literature review of databases such as PubMed, Google Scholar, and ScienceDirect, using search words like "mental health", "COVID-19", "psychological effects", "toxic stress", and "SARS-CoV-2", and included systematic reviews, reviews, case reports, and cohort studies. **Results:** Although it is challenging to quantify the stress people are being subjected to, it is possible to identify how stress affects the body in myriad ways (psychophysiology). Stress disrupts body homeostasis, prompting a cascade of hormones and factors (such as increased cortisol and DHEA) that mount a bodily response. Mental stress has been shown to cause structural changes in the brain, in the hippocampus and amygdala, which can lead to memory disorders and changes in cognition and learning. Long-term activation of the stress response system causes overexposure of cortisol and subsequent deleterious effects throughout the body. Moreover, psychological stress exacts a hidden toll, and chronic stress over time can leave a body more susceptible to not only illnesses, but other acute, stressful events as well, compounding the effect with potential for further harm. Emerging mental health issues from the cumulative effects of this pandemic's psychosocial stressors could become chronic health issues or encourage isolation and increase the stigma that already surrounds mental health. Taken together, it seems that the pandemic's effects are leading to more vulnerable states and worsening of mental health in the general population. **Conclusion**: As the world continues to seek answers to curtail the pandemic and bring life back to normal, attention must be given to how mental health is handled during this crisis.

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It is time to push for integrating mental health with primary care, to treat both mind and body regularly to optimize improvement. Research aimed at understanding the effects of the COVID-19 pandemic on psychological stress is warranted to mitigate the consequences and address mental health properly.

Keywords: Covid-19; stress; mental health; depression; anxiety

Introduction

The emergence of the global coronavirus disease 2019 (COVID-19) pandemic brought with it unforeseen and unprecedented conditions for millions. Conspicuous disorders of the respiratory, gastrointestinal, and neurological systems have taken center stage, but an important category must be brought to the forefront: the psychological and emotional effects of this pandemic. Mandatory nationwide lockdowns, self-quarantining, and understandable anxiety about the unpredictable future are significant stressors and are having both detectable and undetectable impacts on mental and physical wellbeing. Negative affectivity including depression, loneliness, boredom, self-harm, and domestic violence doubled shortly after, as well as financial burden and unemployment. Mental health silently affects everyone and could be a deciding factor in recovery and remission of many health conditions and disorders. This paper discusses the physiological effects of the normal stress response as well as toxic stress; it then goes on to assess the impact of psychosocial stressors and the pandemic on the human body, focusing on the unseen effects of mental health that could be keeping the door open for COVID-19 long after the grueling pandemic has died down.

Background: COVID-19 Pandemic

The coronavirus pandemic (COVID-19) originated in the Hubei province of China in December of 2019. COVID-19 is caused by an enveloped RNA virus named SARS-CoV-2, which gains entry through receptor proteins on the surface known as angiotensin converting enzyme II (ACE2)[1]. The spike-like protein uses the natural physiology of the human body to infect. ACE2 receptors are found all throughout the body, in the skin, liver, intestines, colons, stomach, nasopharynx, kidneys, lymph nodes, bone marrow and more, although it is especially highly expressed in the alveolar tissue of the lungs and vascular system. SARS-CoV-2 forms a bond with the renin-aldosterone angiotensin system that controls many of the physiological responses including homeostasis and blood pressure[2]. The structure of this virus that has plagued the globe has equipped the invasive organism to have a great affinity for the anatomy of the human species. The COVID-19 virus has the ability to suppress the immune system by discreetly penetrating the body without activating the first responders: the macrophages[1]. The ways in which the virus has taken a toll on the human body is more than just transduction, transmission, and infection.

The World Health Organization (WHO) reported that as of November 10, 2024, there have been over 776.8 million confirmed cases, with over 7 million confirmed deaths, reported across 234 countries, areas and territories[3]. The pandemic has affected myriad cultures, people, places, and systems, leading to a mass panic around the world. The impact of COVID-19 on humans is multifactorial, with its effect on mental health alarming[4]. Pandemic events cause not only momentarily negative impact, they also result in long-lasting health problems. During the midst of it, people faced isolation, quarantine, social distancing, mortality, racism, societal dysfunction, and absence of a definitive treatment or vaccine. All of these factors have contributed to generate intense trauma and even today continue to create an atmosphere of toxic stress across the globe[5]-[7].

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The Physiological Effects of Stress and Toxic Stress on the Body

Stress, also known as the "fight or flight" response, or general adaptation syndrome, is a physiological and cognitive natural response to any potential harm the body perceives. It triggers the activation of the hypothalamic-pituitary-adrenal axis (HPA axis) which leads to the production of a vital hormone called cortisol. Cortisol induces behavioral as well as physiological changes in the body[8]. Stressful incidents cause a sudden rise in cortisol level followed by a rapid decrease with the termination of the stressful event. While this elevation in blood cortisol is a protective mechanism, a continuous and significant rise in cortisol due to persistent stress has the ability to turn this protective mechanism into a powerful force that can cause a wide range of physical, behavioral, emotional, and cognitive problems[8].

Toxic stress can lead to an immune dysregulation and a persistent inflammatory state that increases the risk and frequency of infections[5]. Chronic elevation of inflammatory marker proteins damages tissues and increases the risk of diseases such as cardiovascular disease, autoimmune disorders, chronic obstructive pulmonary disease, viral hepatitis, and cancer[9]. Furthermore, it's known that toxic stress is involved in the pathophysiology of depressive disorders, behavioral dysregulation, PTSD, and psychosis[5].

A study about toxic stress history and assessment of HPA axis function reported that toxic social stress during development was related to altered acute HPA response to social stress in adulthood, and that high levels of childhood adversity had a blunted salivary cortisol response[10]. Trauma exposure during childhood has long-lasting effects into adulthood and potentially affects the development of the brain, the neuroendocrine and immune systems, as well potentially impacting life opportunities, resulting in poor outcome of health and well-being[11]. This is an important consideration in tackling the impacts of the COVID-19 pandemic on the mental health of children. There is a significant need to prevent negative outcomes on childhood development, and policies and programs must be implemented to promote awareness and address the short- and long-term effects.

As discussed in the above sections, stress affects the body in a myriad of ways – the psychophysiology is intricate and complex. In addition to disrupting body homeostasis and prompting a cascade of hormones and factors (such as cortisol, DHEA, catecholamines, etc)[12][13] that mount a bodily response, mental stress has been shown to cause structural changes in the brain, particularly in the hippocampus and the amygdala[14]. These can lead to memory disorders and changes in cognition and learning[14]. Long-term activation of the stress response system causes overexposure of cortisol and subsequent deleterious effects throughout the body, including the immune, cardiovascular, gastrointestinal, and endocrine systems[14].

Moreover, psychological stress exacts a hidden toll, and chronic stress over time also leaves a body more susceptible to other acute, stressful events as well[12], compounding the effect with potential for further harm. Various studies in the literature and systematic reviews have shown evidence that responses of pathways such as the HPA axis to acute stress are related to future health outcomes, in terms of both physical and mental health[12].

The Concept of Allostatic Load

Another important concept to consider in discussing the effects of stress on mental health is allostasis, which refers to the process of making physiological changes (through activation of neuroendocrine-immune mechanisms) in response to stressors in order to promote adaptation and maintain stability[13][15]. Adaptation or allostasis often has a cost called allostatic load. Authors McEwen and Stellar[13] further defined the concept of allostatic load, referring to the "strain on the body produced by repeated ups and downs of physiologic response, as well as by the elevated acuity of physiologic systems under challenge, and the changes in metabolism and the impact of wear and tear on a number of organs and tissues, [which] can predispose the organism to disease." Allostatic load can be affected by the entire spectrum of stressors, ranging from daily life experiences to major

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life changes to everything in between, including habitual behaviors such as lack of sleep, poor diet, lack of social engagement, and sedentary lifestyle[15].

McEwen and others have described four response patterns of allostatic load to environmental challenges. The first one is frequent stress, with repeated insults of stressful stimuli leading to allostasis[16]. In the second pattern there is a lack of adaptation to repeated presentation of the same situation–in other words, the organism fails to adapt to the situation. The third type is a situation where the physiologic response patterns remain activated and the allostatic responses fail to shut down even after cessation of the stressful stimuli[17]. The last type of response pattern is due to inadequate activation of primary adaptive responses, where additional compensatory mechanisms are activated to meet the challenge[18].

COVID-19 and Mental Health

During this COVID-19 pandemic, it is possible to see how both acute, minor stressors and stronger, more frequent stressors are affecting much of the general population as numbers of positive cases and the death toll continue to climb steadily since the declaration of the global pandemic in March 2020. The impact of COVID-19 on mental health is alarming, and it affects the human body and mind in a multifactorial manner, partially determined by an interaction between precision brain profiles and the universal threat to human connection posed by the virus[19]. Worries over transmission of the disease and disruption of daily life, coupled with social distancing and isolation in many parts have taken a toll on all people regardless of age, race or background.

Isolation, prevention measures, quarantine, social distancing and mortality generate fear, frustration, stress and anxiety in the population. Furthermore, quarantine, self-isolation and social distancing cause a negative impact on mental health[20]. Social isolation and loneliness can instigate many psychiatric disorders, trigger suicidal behavior and promote unhealthy lifestyle choices such as smoking, alcohol consumption, and poor dietary and physical activity choices. Loneliness can also cause physiological changes in the body, including increased HPA axis activation[21]-[23]. Community anxiety as a whole rises during outbreaks[24][25], and it increases even more with increased reporting in the media and misinformation as the media struggles to keep up with the ever-changing guidelines and scientific research. Previous studies conducted after the MERS and SARS outbreaks have shown that incidences of depression, anxiety and PTSD increased during and after the outbreaks[26], and the severity of emotional distress faced by both the general population and healthcare providers increased[26][27]. A nationwide survey of psychological distress in China during this pandemic showed that 53.8% of respondents rated the psychological impact as moderate or severe, while 16.5% reported moderate to severe depressive symptoms, and 28.8% reported moderate to severe anxiety symptoms[28].

Another important consideration is how those who are affected by the disease or have family members affected by the disease are viewed by those who manage to avoid it: those in affected areas sometimes face social ostracizing and discrimination[24]. This increase in stigmatization can have a broad impact on mental health and feelings of safety, as well as implications for social disruption that can last years[29]. With social distancing and isolation measures being enforced legally in many areas, those who are grieving sudden losses of a loved one due to COVID-19 or other reasons may not have the chance to properly grieve or find closure, and this can lead to long-lasting emotions of resentment or anger[30]. Those with pre-existing conditions who have to receive treatment in isolation or those with mental health disorders who suddenly don't have access to their support systems all face increased susceptibilities and could be at higher risk for COVID-19 infection[27]. Suicide numbers have been potentially linked to the psychological implications of COVID-19 in some countries, such as South Korea and India[31]. An increased risk of suicide has been linked to economic instability–the lockdown measures have resulted in tens of thousands of people losing their jobs, and there is also a link between unemployment and increased prevalence of depression, alcohol or substance use disorders[32].

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The health outcomes of this virus not only affect the general population, but they also affect health professionals working on the front line; it has been shown that they present with medium to high levels of anxiety, depression, nervousness, insomnia, and stress[33]. Furthermore, high-risk populations such as the homeless, elderly, children, people with disabilities, and people with mental health disorders can be further affected or have increased deterioration of their mental health due to the COVID-19 pandemic[20].

Emerging mental health issues from the cumulative effects of this pandemic's psychosocial stressors could become chronic health issues for many, or these issues could encourage isolation and increase the stigma that already surrounds mental health. Taken together, it seems that the pandemic's effects are leading to more vulnerable states and worsening of mental health in the general population. Studies from previous pandemics have shown that the impact of such stressors extends beyond the time period immediately surrounding the pandemic or quarantine situation[34].

Future Scope

This unprecedented pandemic and its far-reaching psychological effects paint a picture of an increasing number of people in more vulnerable states and worsening of mental health in the general population. As the world continues to seek answers to curtail the pandemic and bring life back to normal, attention must be given to how mental health is handled during this crisis. It is time to push for immediate and purposeful integration of mental health with primary care specific to concerns related to the COVID-19 pandemic in order to treat both mind and body to optimize improvement. The high impact of COVID-19 on mental health is a public health priority and demonstrates a need for developing and implementing community-based strategies and policies to support psychologically vulnerable individuals and reduce the burden of disease[35]. Research aimed at understanding the comprehensive effects of the COVID-19 pandemic on psychological stress is warranted to mitigate the consequences and address mental health properly, even years after the pandemic started.

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