Physician Distress and Burnout: The Neurobiological Perspective

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Learning Objectives: On completion of this article, you should be able to: (1) differentiate the neurobiology of how uncontrolled stress, but not controlled stress, contributes to burnout, (2) recognize how the impact of chronic stress on prefrontal cortex regulation may explain several challenges associated with burnout in physicians, including reduced motivation, unprofessional behavior, and suboptimal communication with patients, and (3) describe how organizational efforts to restore control to physicians may be particularly helpful for reducing burnout.

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Abstract

Physician burnout and other forms of occupational distress are a significant problem in modern medicine, especially during the coronavirus disease pandemic, yet few doctors are familiar with the neurobiology that contributes to these problems. Burnout has been linked to changes that reduce a physician's sense of control over their own practice, undermine connections with patients and colleagues, interfere with work-life integration, and result in uncontrolled stress. Brain research has revealed that uncontrollable stress, but not controllable stress, impairs the functioning of the prefrontal cortex, a recently evolved brain region that provides top-down regulation over thought, action, and emotion. The prefrontal cortex governs many cognitive operations essential to physicians, including abstract reasoning, higher-order decision making, insight, and the ability to persevere through challenges. However, the prefrontal cortex is remarkably reliant on arousal state and is impaired under conditions of fatigue and/or uncontrollable stress when there are inadequate or

excessive levels of the arousal modulators (eg, norepinephrine, dopamine, acetylcholine). With chronic stress exposure, prefrontal gray matter connections are lost, but they can be restored by stress relief. Reduced prefrontal cortex self-regulation may explain several challenges associated with burnout in physicians, including reduced motivation, unprofessional behavior, and suboptimal communication with patients. Understanding this neurobiology may help physicians have a more informed perspective to help relieve or prevent symptoms of burnout and may help administrative leaders to optimize the work environment to create more effective organizations. Efforts to restore a sense of control to physicians may be particularly helpful.

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Occupational distress, including professional burnout and moral distress, are widespread problems in modern medicine.[1] These challenges existed before the coronavirus disease 2019 (COVID-19) pandemic and are likely being amplified by the continuing challenges posed by this event. Burnout refers to an occupational syndrome associated with affective and cognitive changes, including emotional exhaustion, depersonalization or cynicism, and diminished feelings of personal efficacy resulting from chronic occupational stress. Burnout is formally recognized by the World Health Organization as an occupational syndrome and increases the risk of hypertension, atrial flutter, cardiovascular disease, depression, and suicide.[2,3] By definition, occupational burnout is primarily precipitated by characteristics of the work environment rather than by individual problems with resilience or coping, and thus changes in the work environment are key to reducing risk.

Large-scale studies suggest that occupational stress and symptoms of professional burnout are more prevalent among physicians than among workers in other fields, even after adjustment for work hours and level of education.[4,5] Burnout can have many professional and personal consequences, including increased physician turnover, reduced quality of care for patients, broken personal relationships, and problematic alcohol use.[5]

The high prevalence of physician burnout has been long-standing, linked to changes in the practice environment that reduce physicians' control over their work, undermine connections with patients and colleagues, interfere with work-life integration, and thus result in uncontrolled stress.[5] In situations like the current COVID-19 pandemic, perceived loss of control and overwhelming workloads can further exacerbate this process. In more typical times, financial pressures and administrative requirements from payers and regulators have resulted in greater productivity demands, increased workload, and reduced independence for physicians in many practice settings. Physicians must also keep up with the rapid expansion of medical knowledge and deal with increased administrative burdens related to electronic health records and regulatory requirements. They also face unprecedented levels of scrutiny from administrators on suboptimal metrics that often fail to recognize the nature of their work (eg, relative value units, patient satisfaction scores, percent of charts closed in 24 hours).

Although it is triggered by characteristics of the work environment, chronic occupational stress ultimately affects biologic function. The lack of control over many stressors in modern medicine can have toxic effects on brain circuitry.[6-8] An appreciation for the ways in which the brain changes in response to uncontrollable stress can help physicians recognize symptoms and lead to constructive personal and organizational interventions. Neuroscientists have discovered that exposure to *uncontrollable* stress—but not controllable stress—has marked deleterious effects on the prefrontal cortex (PFC), the brain region that governs higher cognition and provides top-down control of

thought, action, and emotion[6-8] In this article, we provide a brief review of PFC functions, the susceptibility of the PFC to uncontrollable stress, and how understanding this neurobiology can help physicians and medical organizations develop rational and informed strategies to reduce the risk of burnout.

THE HIGHER FUNCTIONS OF THE PFC

The PFC resides in the frontal lobe, anterior to the motor cortices (Figure 1A). Many of the cognitive operations performed by the PFC[9] are an essential part of a physician's mental toolbox: the PFC governs high-order reasoning, social cognition, and complex decision making, including the integration, conceptualization, and critical evaluation of information. It is essential for executive functions such as attentional regulation, planning and organization, guiding appropriate social behaviors, including placing patients' interests above one's own, and maintaining integrity despite challenges. The most anterior aspects of the PFC govern metacognitive abilities (thinking about thinking) that permit such capacities as insight about oneself and others, moral conscience, emotional intelligence, and empathy—all of which are critical for optimal physician performance. The right PFC is specialized for inhibitory control and dysfunction can lead to inappropriate behaviors or lapses in professionalism, while the left PFC is specialized for language production in most right-handed individuals. The PFC can also act as a "mental cheerleader," motivating higher goals and regulating emotional circuits, including those that mediate mood and anxiety.

STRESS IMPAIRS PFC FUNCTIONING: THE IMPORTANCE OF CONTROL

Although the PFC is capable of remarkable cognitive functions, these cortical operations are very energy-intensive and highly sensitive to the arousal state. As summarized in Figure 2, arousal has an "inverted U" dose-response on PFC function in which the PFC higher-order abilities are weakened both by fatigue and by uncontrollable stress, either of which can take the PFC "off-line" (Figure 1B).[10] Sleep deprivation particularly impacts PFC functioning, with impairments in PFC metabolic and physiologic activity correlating with cognitive deficits.[11] Prefrontal cortex functioning is also impaired by uncontrollable stress exposure, including an acute stressor if the individual feels threatened by the situation. This scenario evokes a series of chemical events in the brain that rapidly disconnect PFC circuits. For example, during incontrollable stress, high levels of norepinephrine and dopamine are released in the brain, which weakens PFC function. These catecholamines initiate intracellular signaling cascades that rapidly open potassium channels near PFC synapses to weaken circuit connections.[10] This process impairs PFC cognitive functions, which can result in diminished working memory and attention regulation, poor decision making, and other cognitive deficits that can be measured in both animals[10,12,13] and humans.[14-16] High levels of norepinephrine and dopamine are also released in more primitive brain circuits such as the amygdala, striatum, and brain stem, where they have the opposite effect and strengthen the unconscious habits and emotional responses that are the purview of these more ancient brain structures.[17-19] These changes can occur very rapidly, for example when one is cut off while driving on the highway, or in response to unexpected, bad news. These alterations in brain physiology may be helpful in the former situation, allowing one to rapidly step on the brakes, but may be detrimental when a complicated challenge requires thoughtful evaluation and guidance by the PFC. In contrast to uncontrollable stress, controllable stressors do not elicit these detrimental chemical actions.[5] Thus, if one feels confident that one can handle a challenging situation or that there are sufficient supports to maintain one's safety, the PFC can inhibit the stress response and maintain a more optimal neurochemical environment.

With sustained uncontrollable stressors there are additional, more substantial, changes in brain circuits. Chronic uncontrollable stress causes PFC synaptic connections to atrophy, while those in more primitive brain circuits

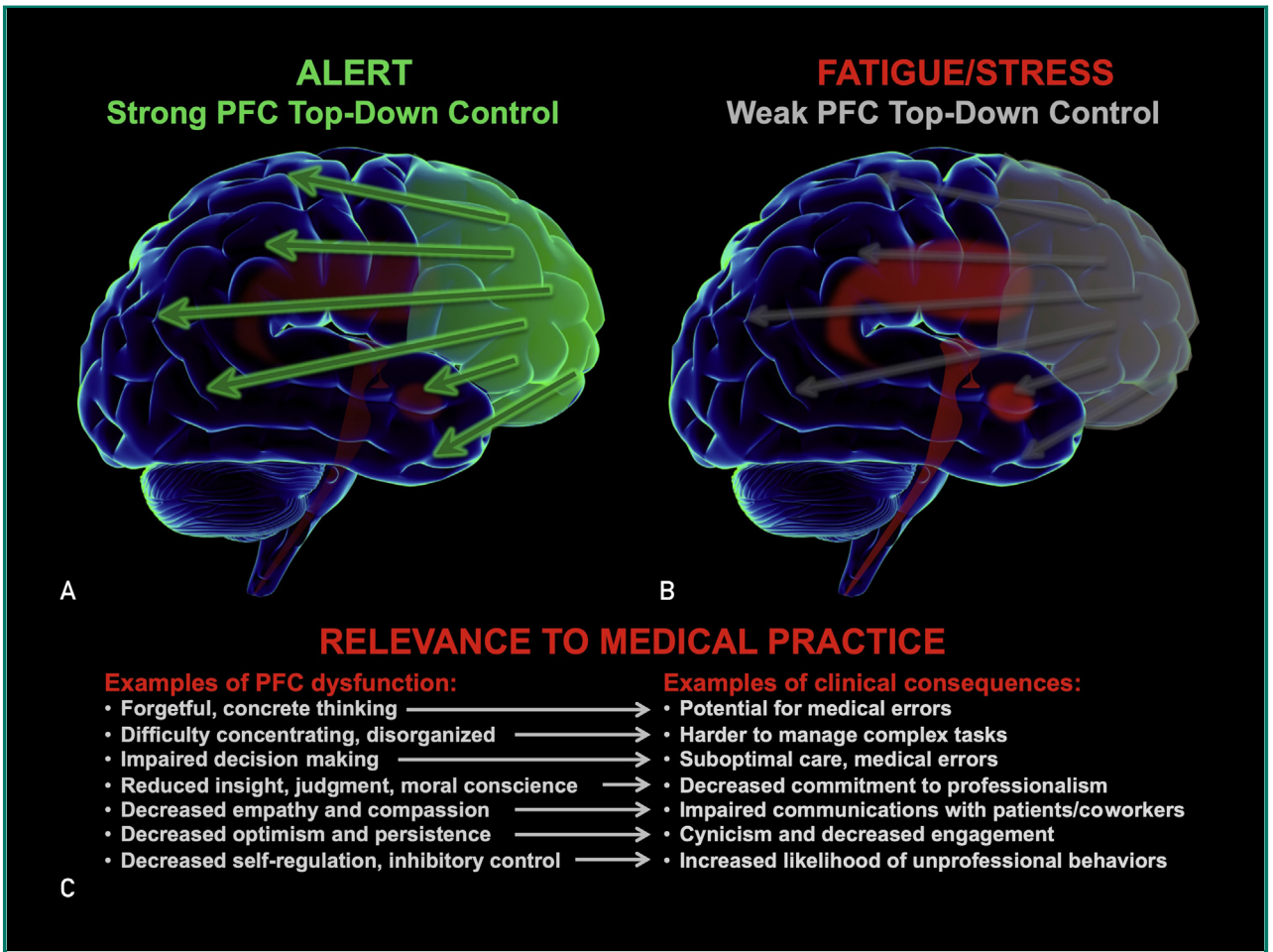

FIGURE 1. The higher cognitive functions of the prefrontal cortex (PFC) are impaired by fatigue or uncontrollable stress, posing potential ramifications to clinical practice. A, The PFC (highlighted in green) resides in the brain's frontal lobe, anterior to the motor cortices. The PFC has extensive connections with cortical and subcortical brain areas that provide top-down control over thought, attention, action, and emotion when we feel rested, interested, and in control. B, Under conditions of uncontrollable stress or fatigue, PFC connections are weakened (gray), and there is a loss of top-down control and impaired PFC cognitive functions. Stress also activates more primitive brain circuits (highlighted in red) that mediate unconscious responses and habits. Chronic stress exposure causes atrophy of PFC connections, weakening the thoughtful, evaluative responding needed for professional and personal fulfillment. C, Examples of some of the cognitive changes that occur with PFC dysfunction and their potential consequences to physician performance. For a brief summary of these neurobiological mechanisms, see the Yale Medical School YouTube channel at www.youtube.com/watch?v=vdDvChLuQsA .

expand, a phenomenon documented in both animal and human brains.[12,13,20-22] This work is directly relevant to the syndrome of burnout, as humans with occupational exhaustion have thinner PFC gray matter[8] and have to recruit larger volumes of PFC function to maintain the same levels of cognitive performance.[23] Although these physiologic studies were not performed in physicians, they represent fundamental human biology and are thus applicable to burnout in doctors as well. Fortunately, animal and human studies reveal that PFC connections can regrow during sustained periods of nonstress, allowing the return of top-down control.[8,10,12,24]

THE RELEVANCE OF IMPAIRED PFC FUNCTION TO OCCUPATIONAL BURNOUT

Just as it is useful to understand the mechanisms by which the immune system, which is typically our ally, can inappropriately attack

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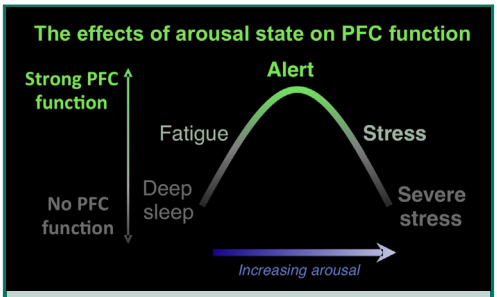

FIGURE 2. The effects of arousal on prefrontal cortical (PFC) function. The arousal state has an "inverted U" dose-response effect on PFC functioning. The PFC synapses require stimulation from the arousal systems (acetylcholine, norepinephrine, dopamine, serotonin) in order to function properly, and inadequate levels (eg, during fatigue) weaken PFC function. Conversely, excessive norepinephrine and dopamine release during uncontrollable stress also weakens PFC function by rapidly weakening PFC synaptic connections. It is noteworthy that caffeine increases the release of acetylcholine in the PFC, which may explain why it can be helpful to cognitive function in rested individuals.

the body in an autoimmune disorder, it is helpful to know the molecular mechanisms that actively weaken higher brain circuits during uncontrollable stress. This neurobiological perspective provides a rational understanding of symptoms and can inform strategies for prevention and treatment. Impaired PFC self-regulation may explain a number of the challenges associated with occupational burnout, such as reduced motivation, unprofessional behavior, decreased compassion, and suboptimal communication with patients (Figure 1C). During a time of intense workload, such as a global health emergency, physicians and other health care professionals may be under extraordinary stress. Evidence indicates that having a sense of control can protect against cognitive deficits during stress exposure.[14] Thus, understanding that changes in mental state are part of the natural neurobiological response may provide perspective and a sense of control, especially with the knowledge that PFC connections and function can be restored when the stressor abates.

Building emotional intelligence skills can also increase control by enhancing self-awareness as a means to enhance self-regulation and social management.[25,26] Recognizing when work demands have become depleting or are triggering frustration allows individuals to be aware of their needs and make choices over the dimensions they do control, such as naming emotions (ie, frustration, exhaustion, anger, moral distress, grief), taking a break to attend to physical needs (hunger), and increasing prioritization of sleep or other needs. Strengthening social awareness as a means to attending social management can also help physicians more effectively support colleagues dealing with uncontrolled stress.

Awareness of the neurobiology and focus on short-term responses can set the stage for rational longer-term actions. Specifically, opportunities for clinicians to regain control (eg, creating organization and structure in a time of chaos, advocating for change, the ability to identify inefficient processes and lead efforts to improve work flows, working part-time as a means to enhance control) may help relieve burnout symptoms.[5] A sense of control can also be enhanced by gaining perspective, perhaps by engaging in activities that are meaningful and refreshing (eg, recognizing meaning and purpose in serving patients and society, mindfulness-based stress reduction, recreational exercise), and by learning about the underlying neurobiology of the stress response, which can help reduce self-blame and promote a more compassionate view of oneself and others.[27] Deliberate decisions to foster work-life integration can also increase perceived control. Professional coaching is a strategy for physicians that is proven to advance such efforts.[28]

Additional behaviors that respect the physiological needs of the PFC may also have an impact. Exercise and healthy diet and snacks can support the high-energy demands of the PFC. Maintaining these activities, despite intensive workloads, should be a priority to facilitate efficacy over an extended interval. In contrast, alcohol consumption, while offering temporary relief from stress, can worsen PFC physiology in the long run.[29] It is also important to recognize when occupational stress has become

more global distress (such as depression[30]) because proper treatment (eg, selective serotonin reuptake inhibitors or psychotherapy) has been found to restore balance in PFC circuits and function.

UNDERSTANDING THE NEUROBIOLOGY CAN GUIDE SYSTEM-BASED STRATEGIES TO REDUCE BURNOUT

A better understanding of the neurobiology of uncontrolled stress also has implications for organization and system efforts to reduce burnout by improving medical practice environments. Efforts to restore control to physicians may be particularly helpful, even under conditions in which an overwhelming workload taxes the entire system.[31] Such efforts may involve changes in the behavior of organizational leaders, regularly asking physicians for input, providing them greater voice in decision making, developing and providing clear structure to rapidly expanded care teams, and providing authentic opportunities to organize and shape their working conditions.[5] These opportunities could include incorporation of stress-reducing periods such as breaks, which can be facilitated by means of scheduling and creation of physician break rooms or respite spaces. In more typical times, such opportunities also include choice and flexibility of work schedules, the ability to lead workflow redesign, and compensation systems that incentivize, rather than discourage, taking vacations.[5,31] Supporting activities that provide and enhance social supports (fostering collegiality, for example, or developing peer support programs) and that provide meaning in work (eg, professional development, mentorship, adequate time to develop connections with patients) provide perspective and purpose that also enhance the perception of control.[32]

The physician and health care workforce was plagued with a high prevalence of burnout and occupational distress even prior to the COVID-19 pandemic.[33] A lack of control precipitated by the abrupt and dramatic increase in professional workload, unpredictability of the surge in patients with infection, deployment of physicians to areas outside their expertise, exposure to suffering, and inability to reverse the disease process for many patients can all contribute to an acute exacerbation of this chronic problem that will likely persist after the pandemic. An understanding of the neurobiology of burnout and the importance of control may allow administrative leaders to identify the characteristics of the work environment that contribute to occupational stress and identify opportunities to increase physicians' sense of control to create more effective organizations.

Abbreviations and Acronyms: **COVID-19** = coronavirus disease 2019; **PFC** = prefrontal cortex

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