

When Stress becomes Hopelessness

Joshua Minks*

Jonas Veterans Health Scholar, University of Missouri, United States of America

***Corresponding Author:** Joshua Minks, Jonas Veterans Health Scholar, University of Missouri, United States of America.

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Today, we face uncertainty in the outcomes of very influential events. Events resulting as consequences from a series of choices like the ominous butterfly effect that can turn mere moments in time into a perfect storm. Social unrest from a series of poor choices made by law enforcement officials resulting in peaceful protests or looting. Civic uncertainty regarding economic factors and infection control in the face of a pandemic resulting in greater use of technology or bold defiance of COVID-19 prevention measures with increasing morbidity and mortality rates. The political response seeming timely and opportunistic for influential men and women to speak against the motives of their opponents leaving voters to feel empowered or ambivalent.

These events and the choice of responses are not so different from those of historical events. The plight of the Revolutionary War left early Americans ready to fight for freedom or endure tyranny. The Civil War split a country for or against slavery with white landowners needing to choose between the ideal of equality or greed at the expense of slavery. Unfortunately, cultural and social differences among people continue to influence acts of aggression by one against another that expresses different values or beliefs. Many notable political leaders - Washington, Lincoln, Grant, King, Johnson, Wilson, and others - chose to speak out against oppression, against antagonists for change. The colloquial belief is that everyone has a choice; however, these political leaders, you, I, everyone has had influential moments in our upbringing that taught us what is right and wrong...according to us. We perceive our world as we choose.

With our aptitude for learning coupled with conceptual processing, human beings are capable of overcoming great challenges; however, we at times can be overwhelmed by what we perceive as absolute truths or impassable barriers. The folly of which is rationalizing our response to circumstances from a sense of hopelessness. Questions that arise include: How does one get to a point of hopelessness and can it be identified?

To understand how an individual reaches a state of hopelessness, a deeper understanding of the nature of challenge and threat appraisals is needed. Lazarus and Folkman [1] suggested that the latter demands greater physiological adaptation in terms of stress hormones and compromises morale, quality of functioning, and somatic health. While challenge and threat appraisals are distinctly different in terms of their impact on cognitive components such as morale, individuals can experience both threat and challenge emotions.

This makes a subjective assessment of emotional expression alone insufficient in understanding how an individual is coping with stressful circumstances. At best, an individual's expression and posture require objective assessments such as electrocardiogram and facial electromyography to interpret the relationship of those features with an individual's expressed emotions [2]. Not to mention, individuals may convey confidence in an effort to mask a threat response [3]. For providers trying to determine how their patients are coping with stressful circumstances, a subjective assessment of observed emotions alone is not sufficient to understand how a patient is coping.

If time is permitted and stressors continue without swift resolution, the consequences could be severe in terms of the physical cost associated with adaptation. Physical adaptation occurs in direct response to the stressor, releasing glucocorticoids (GC), the primary response for physical and psychological stressors [4]. Whether the stressor repetitively occurs in relation to external factors such as physical pain or internal factors such as depression or anxiety, an individual may appraise the stressor as uncontrollable [1].

In this case, the secretion of GC cascades and the body's systems slowly succumb to the negative effects of excess GC in the system such as metabolic syndrome, hypertension, and osteoporosis [5]. While Barbot, *et al.* [5] indicates that the systemic effects - Cushing's syndrome - results predominantly from GC therapy or tumors, literature suggests that stress from other sources such as depression can produce comparable effects to GC therapy with higher basal GC levels [6].

The physiological presentation of hopelessness appears to be the state when GC levels return to base levels prior to the presence of stressors that were appraised as threats. This occurs when an individual has a high stake in the outcome or strong belief that the individual can control the outcome [1]. Determining a state of hopelessness by observation may be as difficult as determining if an individual appraises a situation as a challenge or a threat. While a flat affect or unresponsiveness may appear to be synonymous with hopelessness, such signs may merely be representative of melancholia and not necessarily hopelessness. Studies on melancholia remain inconclusive regarding the relationship between melancholia and GC levels; GC levels remained elevated despite dexamethasone testing for melancholic and non-melancholic patients [6].

Elevated GC levels cause GC receptor activation, particularly in the limbic system which includes the hippocampus and amygdala. While the amygdala activates the HPA axis via excitatory afferents, the hippocampus suppresses the stress response via inhibitory afferents [7]. With excess GC in the body, genomic changes can occur secondary to the action of GC response elements in gene regulatory regions (Rein, *et al.* 2020).

Neuronal activity is compromised as a result of an inability to repolarize for effective signal transduction among the hypothalamus, as part of the HPA axis, the hippocampus, and the amygdala [7]. While the genomic changes suggested by Rein, *et al.* (2020) don't specify that the genomic changes in the hippocampus could lead to atrophy, the compromised brain function that can result from a period of elevated GC levels is suspicious for such an outcome. If hippocampal atrophy does occur as a result of elevated GC levels, the outcome could explain the state of hopelessness.

The state of hopelessness could result from unresolved stressors that an individual initially perceives as threats. The stressors may be repetitive or cumulative in nature, leading an individual to believe that resolution is not feasible, and the demands for physiological adaptation require chronic elevation of GC levels. Such stressors may include loss of work or severe illness associated with COVID-19, social injustice or system racism associated with law enforcement, and fear of political malfeasance at the cost of social wellbeing. Whatever the cause, hopelessness may as well be synonymous with false bravado as individuals may be willing to adapt at any social cost when they believe they have nothing to lose.

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