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The Gravity of Weight

The Obliterative, Dislocating Effects of Stress

Mapping out sorrow: from homeostasis to allostasis and allostatic load.

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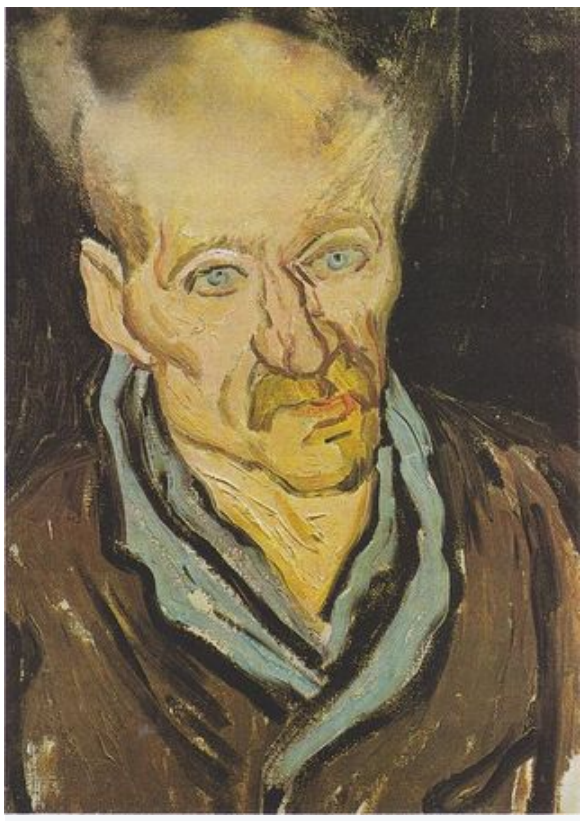

Vincent van Gogh, "Portrait of a Patient in the Hospital Saint-Paul. 1889, van Gogh Museum, Amsterdam.
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Grief has "the power to derange the mind," wrote Joan Didion in response to experiencing the sudden death of her husband, in her powerful book, *The Year of Magical Thinking* (2005). When death is sudden, we might expect to feel shock, she wrote, but "We do not expect this shock to be obliterative, dislocating to both body and mind." Didion poignantly revealed how crazed and impaired were her cognitive functions: "I could not give away the rest of his shoes: he would need his shoes if he was to return." And when the autopsy report she had requested immediately after his death came a year later, she realized she had inadvertently put the incorrect address, using their original address from just after she and her husband had married 40 years previously, on the hospital's request form.

Likewise, C.S. Lewis, also upon the death of his beloved wife, writes, "No one ever told me grief felt so like fear" (*A Grief Observed*, 1961). He described feeling there was "an invisible blanket between the world and me" in which he found it hard "to take in what anyone says." He continues, "I thought I could describe a state; make a map of sorrow. Sorrow, however, turns out not to be a state but a process. It needs not a map but a history..."

Both Didion and Lewis faced what Rockefeller University neuroscience researcher Bruce McEwen describes as "perhaps the ultimate social stressor" (*The End of Stress as We Know It*, 2002), the agony of bereavement.

Jules Charles Boquet, "Mourning, "Musee des Beaux-Arts de Rouen, date unknown.
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What is stress and how can it have such an effect on both body and mind? Stress is "the pressure that life exerts on us and the way this pressure makes us feel," according to McEwen. Essentially, stress is a real or subjectively perceived threat to our "physiological and psychological integrity" (Picard et al, *Nature Reviews Endocrinology*, 2014). Stress is a state of mind (McEwen, *Proceedings of the National Academy of Sciences*, 2012), and it is the brain that determines whether something seems threatening, uncertain, out of control, and hence stressful (McEwen, *Chronic Stress,* 2017; Peters et al, *Progress in Neurobiology*, 2017). *Stress* is the physiological response whereas a *stressor* is the "evocative agent" (Mason, *Journal of Human Stress*, 1975). Further, no two people experience the environment in the same way, (McEwen and Wingfield, *Hormones and Behavior*, 2010), and what is stressful to one person is not necessarily to another.

Acutely, the feeling of stress can mobilize and protect us ("flight or fight" reaction), but when chronic, it becomes pathological and wreaks havoc on mind and body. Stress, though, can be good, called *eustress*, when someone rises to a challenge or takes a risk that leads to a positive outcome; it can also be tolerable in which a person can still cope. Stress,

though, is toxic when someone becomes unable to cope (McEwen, *Annals of the NY Academy of Sciences*, 2016). The ability to adapt to stressors and cope with environmental challenges is *resilience* and the mark of a healthy-functioning brain (Karatsoreos and McEwen, *F1000 Prime Reports,* 2013).

Otto Gutfreund, "Anxiety," 1911-12.
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"A distraught Shiva carrying the body of his wife."
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It was Hans Selye back in the 1930s (*Nature,* 1936) who described a *general adaptation syndrome as* when an organism was exposed acutely to *non-specific* noxious agents (e.g. cold, surgical injury, excessive exercise, or sub-lethal doses of drugs.) Selye did not use the word *stress* until his later writings and distinguished this *general reaction* consisting of alarm, resistance, and exhaustion that was elicited by many different agents from *specific* adaptive reactions such as the muscular development that results from exercise (Selye, *Journal of Allergy and Clinical Immunology,* 1946). Still later (Selye, *Journal of Human Stress,* 1975), he emphasized that stressors can cause different effects in different people depending on internal (e.g., genetics, age, sex) or external (e.g., treatment with drugs, environmental or dietary) factors. He understood the syndrome as the effort of the organism to adapt to a new condition. Selye, though, focused on physical stressors and "underestimated the role of psychosocial influences," that can have obvious substantial impact (Peters et al, 2017). For humans, life experiences, such as bereavement, are the most common stressors (McEwen, *Annals of the NY Academy of Sciences*, 2016).

The implication is that stress causes a disruption in a person's equilibrium or *homeostasis,* a term first used by physiologist Claude Bernard in the mid-19th century and popularized in the medical literature by Walter B. Cannon in the early 20th century. "No single concept has been more central to the development of physiological thought than the principle of homeostasis," says Moore-Ede, who describes it as those "specialized mechanisms unique to living systems which preserve the internal equilibrium in the face of an inconstant world." He thought of Cannon's view as *reactive homeostasis* in which the body took corrective actions *only after* the physiological system had been disturbed. Moore-Ede extended Cannon's concept to include *initiating* corrective responses, often related to circadian rhythms, *in advance of a challenge,* what he called *predictive homeostasis*.

Over time, though, researchers began to appreciate that the concept of homeostasis had its limitations and did not account for the need for "altered responsiveness," i.e., "customization" when exposed to an unpredictable environment and potentially stressful events (McEwen and Wingfield, 2010). Sterling and Eyer (*Handbook of Life Stress, Cognition and Health*) wrote of a "new paradigm" they called *allostasis*, a "far more complex form of regulation than homeostasis" that involves a "continuous re-evaluation of need" and hence continuous readjustments "rather than establishing equilibrium around a specific set point." For these researchers, homeostasis involved maintaining stability and keeping "all the parameters of its internal milieu constant." Humans, though, do not have a constant milieu (e.g., there is a range of blood pressure readings, states of sleep and wakefulness, or states of satiety) and must be able to move flexibly from one state to another in order to achieve stability. For the model of allostasis, health is seen as a state of responsiveness in anticipation of need.

McEwen and colleagues define *allostasis* essentially as achieving stability through change (McEwen and Wingfield, 2010). Successful allostasis involves "minimizing wear and tear" on the body by the "efficient turning on and shutting off" of those mediators of the stress reaction (e.g., cortisol secretion, blood pressure changes, inflammatory responses) (Juster et al, *Neuroscience and Biobehavioral Reviews*, 2010; Peters and McEwen, *Physiology & Behavior*, 2012). The “cardinal feature” of allostasis is that it allows for a wide variation in the levels of these stress mediators that may be needed acutely to cope with “unique experiences” within a varying environment. If released chronically, though, these mediators may ultimately lead to disease (e.g., hypertension, Cushing’s disease, or metabolic syndrome) (McEwen and Wingfield, 2010).

Carlton Alfred Smith, "Recalling the Past," 1888
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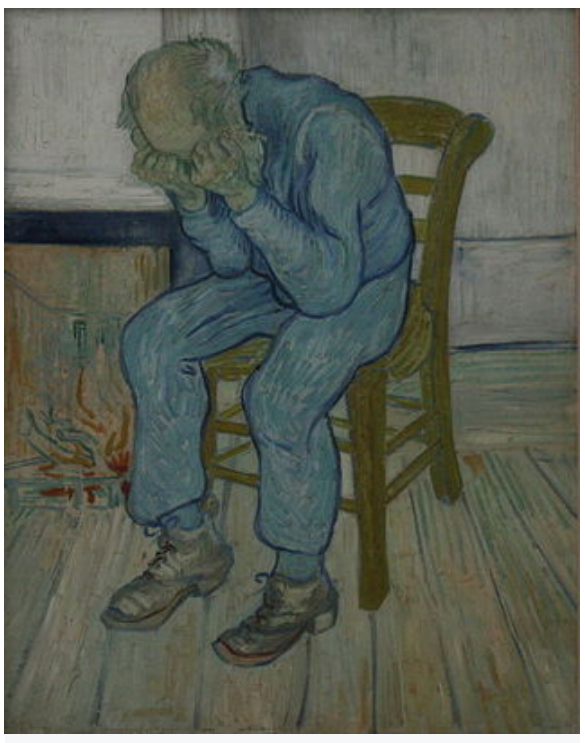
It was McEwen in the early 1990s who coined the term *allostatic load* to refer to the “sequelae of overactivity and dysregulation” of allostasis due to chronic stress (Peters and McEwen, 2012). In other words, “adaptation has a price,” and that price can sometimes lead to allostatic load (McEwen, *Annals of the New York Academy of Sciences*, 1998). An extreme form of allostatic load occurs when this dysregulation is seen in the context of behaviors detrimental to health (e.g., smoking, increased food consumption, lack of exercise, excessive alcohol intake) (Picard et al, 2014). To assess allostatic load, clinicians may request a 12-hour urine collection of norepinephrine, epinephrine, and free cortisol; saliva for cortisol; blood collection for a cholesterol profile and glycosylated hemoglobin, as well as markers of inflammation such as IL-6, C-reactive protein and fibrinogen; waist-to-hip ratio; blood pressure; and heart rate (McEwen and Wingfield, 2010). Furthermore, allostatic load, as evidenced by the sustained increase in cortisol secretion, can have a major impact on brain functioning: The prefrontal cortex, a region involving executive functioning, is particularly vulnerable and may result in deficits in working memory, inhibitory control, and cognitive flexibility on certain tasks (Ottino-González et al, *PsyArXiv Preprints*, 2018). Repeated stress can lead to atrophy of the hippocampus, a structure responsible for episodic and declarative memory (McEwen, 1998; McEwen, 2012) and loss of postsynaptic dendritic spines and shrinking of dendritic branches in parts of the cortex and hippocampus (Peters et al, 2017). In other words, allostatic load represents a "multisystem physiological dysregulation" affecting body and brain (Wiley et al, *Psychosomatic Medicine*, 2016).



van Gogh, "At Eternity's Gate," Saint-Remy, 1890, Kroller-Muller Museum (The Netherlands)
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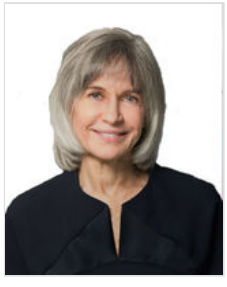
Most recently, McEwen and colleagues (Picard et al, *Psychosomatic Medicine*, 2017; Picard and McEwen, *Psychosomatic Medicine*, 2018) have hypothesized that mitochondria, the “powerhouse” within cells, may be both modulators and targets of the stress response. For example, under stress, mitochondria can swell and their membranes become distended. Apparently, mitochondria can also "sense" levels of glucocorticoids, and mitochondrial dysfunction (e.g., mitochondrial fragmentation) can result from hyperglycemia (Picard et al, 2014), and "faulty" mitochondria can "promote" inflammation both directly and indirectly (Picard et al, 2017). It is also speculated that mitochondria may be involved in the “stress-buffering” effects of exercise (Picard and McEwen, 2018).

Bottom line: Stress is a state of mind: it is a real or perceived threat to our physical and psychological well-being. Acute stress can mobilize our “flight or fight” mechanisms, protect us from sudden changes in our internal or external environment, and enable us to adapt. Our ability to cope with and respond to these vicissitudes is evidence of a healthy-functioning brain. Even for the most resilient, though, chronic stress, whether due to physical or psychosocial experiences, potentially generates what has been called an allostatic load, i.e., a complete dysregulation of all physiological systems, and when extreme, is inevitably obliterative, dislocating, and fundamentally detrimental to both mind and body.

About the Author



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