The new science of stress

The End of Stress as We Know It
by Bruce McEwen, with Elizabeth Norton Lashley
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Reviewed by Thomas G Pickering

Everyone thinks they know the meaning of the word ‘stress’, but its precise definition remains elusive. Bruce McEwen is a distinguished neuroscientist who has dedicated more than 30 years of his career to studying the effects of stress on the brains and hormones of animals, and has summarized his work in this very readable book.

To define the stress response, McEwen uses a term—allostasis—that is probably unfamiliar to most people. Whereas homeostasis is the process by which bodily functions are maintained, allostasis is the process by which they change in response to environmental challenges. The best-known example of this is the fight-or-flight response, which operates primarily through the sympathetic nervous system and the hypothalamo-pituitary-adrenal (HPA) axis.

McEwen's basic thesis is that when allostasis is moderate, it has beneficial effects that help us cope with the stresses of daily life, but when it is excessive or prolonged, it has adverse effects—called the ‘allostatic load’—that lead to wear and tear on the system, resulting in chronic mental and physical disease. He reviews three areas to support his thesis: the cardiovascular system, the immune system and the brain.

Moderate stimulation of the cardiovascular system activates the sympathetic nervous system and mobilizes energy. But stimulating the system excessively can increase blood pressure and lead to atherosclerosis. Moderate allostasis also enhances the immune response, but excessive allostatic load suppresses immunity.

An elegant example of this comes from work done in McEwen's lab, where rats were exposed to a chemical antigen. When exposed to moderate stress, the rats showed a greater inflammatory response, but exposure to the stressor for several weeks suppressed that response. In the brain, moderate allostasis promotes attention and memory storage, but excess stress impairs memory and leads to the loss of nerve cells.

A central player in the brain is the hippocampus, which McEwen's early research showed to be part of the HPA axis, and which is replete with glucocorticoid receptors. Apart from its role in memory and emotion, the hippocampus normally acts to shut off the HPA axis. But excessive exposure to glucocorticoids can cause the hippocampus to shrink, disinhibiting the HPA axis and resulting in a vicious cycle of unfettered allostatic load.

The good news here is that this process is reversible. One of McEwen's postdoctoral fellows found that the adult rat hippocampus continues to produce new nerve cells, particularly in the dentate gyrus. Later experiments in tree shrews showed that a single hour’s exposure to stressors can suppress this neurogenesis, but when the stressor is removed, nerve cells can once again be produced. Dentate gyrus neurogenesis is also reduced with aging, but again, this can be reversed in rats by removing the adrenal glands.

McEwen emphasizes that this is not a prescriptive book and has no eight-week plan for stress-free living. But in the second half of the book, he does discuss practical ways of preventing the ravages of allostatic load—exercise, a good night’s sleep, a good diet and social support. This may sound like motherhood-and-apple-pie advice, but he gives interesting justifications for them, frequently from animal studies. Exercise is one example: mice that have access to running wheels not only show a greater production of new neurons in the hippocampus, but also perform better in maze tests. Diet is another: rats fed a high-fat diet have higher cortisol levels, which take longer to return to baseline levels when the animals are subjected to stress.

In the latter part of the book, McEwen introduces the concept of positive health, which is the process by which the body can prevent allostatic load from descending into allostatic load. Mediators of these protective effects include endorphins and oxytocin, but one of the most intriguing ones is brain-derived neurotrophic factor (BDNF). BDNF has many functions, including protecting the brain from ischemic damage and promoting memory, and its level is increased in rats that exercise regularly. McEwen suggests that BDNF may be one mechanism by which exercise benefits the aging brain.

I found this book to be a compulsive read. Although it is aimed at the general public, it is a serious work that will appeal no less to medically sophisticated readers. And for those of us whose curiosity is aroused by this narrative, there is a comprehensive list of journal references at the end of the book.