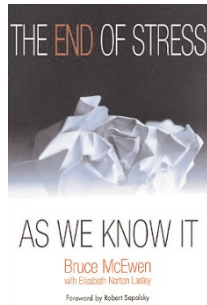


# Your brain on stress



## *The End of Stress as We Know It*

by Bruce McEwen with Elizabeth Norton Lasley  
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*Reviewed by John E. Spiro*

Do grant renewals, teaching responsibilities or troubling newspaper headlines stress you out? If so, a book about stress from Bruce McEwen of Rockefeller University with science writer Elizabeth Lasley may be worth squeezing into your busy schedule.

The authors outline how the 'flight or fight' stress response is normally adaptive—as it shifts energy from long-term to immediate needs. Heart and breathing rates increase, blood vessels in the skin constrict (presumably to reduce blood loss in case of injury), and the immune system is primed to respond; the brain orchestrates these events through signaling cascades that release adrenaline and then cortisol from the adrenal glands. Feedback to the brain, including direct effects of cortisol on the hippocampus, ensures that stressful or highly emotional events are keenly remembered (which is probably adaptive for the next time a similar stressor occurs). Feedback cascades also ensure that the response is turned off appropriately, and that energy stores depleted by the adrenaline rush are replenished.

A combination of genetics and lifestyle choices (poor diet, too little sleep, not enough exercise), however, can lead to an abnormal stress response; among other results, levels of cortisol can remain chronically high. Over time, the stress response, which is protective in the short term, instead can damage the cardiovascular and immune systems and the brain. McEwen gives the example of salmon returning upstream to spawn, a trip initiated and sustained by high cortisol levels. Elevated cortisol boosts the fishes' energy for their (last) journey, but it also kills them via chronic effects on their digestive and immune systems. Although this is of

course an extreme example (and the stress here has adaptive value), the analogy has some weight because both brain and peripheral elements of stress responses are similar in teleost fishes and humans.

The strongest chapters are on the effects of stress on the brain—both the initiator and a target of the stress response. A theme of particular interest is that brain regions activated adaptively by the stress response (the hippocampus and amygdala, for example) also suffer disproportionately (because they have high levels of cortisol receptors) when stress levels stay high. Because the hippocampus is involved in shutting down the hormonal stress response, damage to the hippocampus can also start a vicious cycle.

McEwen tells a story rich with historical anecdotes, integrating research on animals with clinical data. For example, he describes the early resistance to and then experimental proof for the idea that the brain has receptors for chemicals produced by the glands. (It was supposed to be the other way around.) And he chronicles how Phillip Landfield and others helped to connect memory loss, aging and chronic stress by showing that removing rats' adrenal glands could slow age-related memory loss. McEwen also describes how Robert Sapolsky found that exposing rats to corticosterone (their version of cortisol) accelerated aging of the hippocampus. (Sapolsky, a student with McEwen in the 1980s, wrote the foreword to this book.)

In explaining how chronic stress can damage the brain, McEwen puts particular emphasis on the link between elevated stress levels and decreased neurogenesis and dendritic remodeling in the dentate gyrus of the hippocampus. He draws on evidence ranging from experiments on tree shrews exposed to stress to patients with Cushing's syndrome, in which a pitu-

itary tumor causes chronic elevated cortisol levels. He tries to link stress, decreased neurogenesis (resulting in a smaller hippocampal volume), and memory and emotional disturbances, such as posttraumatic stress disorder (PTSD). The idea, though provocative, is intensely debated, and the link is by no means proven. Although growing evidence suggests that new neurons in the adult hippocampus indeed become functional and that a reduction in new neurons can be associated with impaired performance in some tasks, twin studies also caution against extrapolating this data too far. For example, smaller hippocampi might increase the vulnerability to PTSD, as opposed to a situation where trauma causes small hippocampi, which then leads to PTSD.

Through reference to the animal literature and largely anecdotal evidence in humans, McEwen tries to draw a distinction between 'hardship' and 'stress.' The former does not necessarily lead to chronically elevated cortisol levels, and the latter he sees as a particularly acute problem in our modern world, as a result of lifestyle choices and changes in social structures. McEwen prefers the term "allostasis" for the way the brain and glandular systems normally allow the body to respond transiently to a stressful event (analogous to the concept of homeostasis); "allostatic load" then refers to factors that perturb the normal balance. He outlines how many elements of the modern lifestyle feed directly into this load. For example, sleep deprivation and a high-fat diet both raise cortisol levels and may otherwise perturb the stress response. And exercise may have the opposite effect—perhaps, McEwen hints, through a link to neurogenesis.

The authors partly succeed at the difficult task of writing for both general and specialized audiences—although general readers drawn to the book by the title or dust jacket might be disappointed after wading through the detailed science to find no magic bullet 'to end stress as we know it'. And specialists may be frustrated by some of the gaps between the insights from basic research and their potential medical benefits, and by repetition, presumably aimed at making the book more approachable. Nevertheless, the authors contribute to a growing and welcome 'neuroscience news you can use' genre. They even tackle some broad issues like stress caused by socioeconomic inequalities, which may make the book of interest to policy makers.

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