

# Allostasis and Allostatic Load: Implications for Neuropsychopharmacology

Bruce S. McEwen, Ph.D.

*The primary hormonal mediators of the stress response, glucocorticoids and catecholamines, have both protective and damaging effects on the body. In the short run, they are essential for adaptation, maintenance of homeostasis, and survival (allostasis). Yet, over longer time intervals, they exact a cost (allostatic load) that can accelerate disease processes. The concepts of allostasis and allostatic load center around the brain as interpreter and responder to environmental challenges and as a target of those challenges. In anxiety disorders, depressive illness, hostile and aggressive states, substance abuse, and post-traumatic stress disorder (PTSD), allostatic load takes the form of chemical imbalances as well as perturbations in the diurnal rhythm, and, in some cases, atrophy of brain structures. In addition, growing evidence indicates that depressive illness and hostility are both associated with cardiovascular disease (CVD) and other systemic disorders. A major risk factor for these conditions is early childhood experiences of abuse and*

*neglect that increase allostatic load later in life and lead individuals into social isolation, hostility, depression, and conditions like extreme obesity and CVD. Animal models support the notion of lifelong influences of early experience on stress hormone reactivity. Whereas, depression and childhood abuse and neglect tend to be more prevalent in individuals at the lower end of the socioeconomic ladder, cardiovascular and other diseases follow a gradient across the full range of socioeconomic status (SES). An SES gradient is also evident for measures of allostatic load. Wide-ranging SES gradients have also been described for substance abuse and affective and anxiety disorders as a function of education. These aspects are discussed as important, emerging public health issues where the brain plays a key role. [Neuropsychopharmacology 22:108–124, 2000] © 1999 American College of Neuropsychopharmacology. Published by Elsevier Science Inc.*

KEY WORDS: Homeostasis; Stress; Depression; PTSD; Substance abuse; Cardiovascular disease; Hostility; Anxiety; Development; Socioeconomic status

Diagnosable mental disorders affect approximately 22% of the adult US population in any given year, and the costs associated with treating these disorders was estimated almost a decade ago to be \$74 billion, with an additional estimated indirect cost of the same magnitude for lost productivity. Clearly, the total costs are much greater now as we approach the year 2000! Affective

and anxiety disorders are estimated to account for almost half of the cost burden of these disorders (Rupp et al. 1998). Stress plays a role in mental disorders, as both a causal factor and an outcome of disordered thought and disrupted interpersonal relationships (for discussion of major depression in this regard, see Kessler 1997).

In spite of the wide-spread recognition of these relationships, medical science has been struggling for decades to understand the relationship between stress and disease. Stress may be defined as a threat, real or implied, to the psychological or physiological integrity of an individual. However, the widespread use of the term "stress" in popular culture has made this word a very ambiguous term to describe the ways in which the body copes with psychosocial, environmental, and physical challenges. One reason for this ambiguity is that the subjective experience of stress does not always

From the Laboratory of Neuroendocrinology, The Rockefeller University, New York, NY.

Address correspondence to: Bruce S. McEwen, Ph.D., The Rockefeller University, 1230 York Avenue, New York, NY 10021.

Received June 27, 1999; revised September 28, 1999; accepted September 30, 1999.