Stress leads to a multitude of chronic diseases, whereas exercise has a health-enhancing impact. One possible reason for the preventive effect of exercise may therefore be that exercise results in a reduced stress reactivity. Concretely one might suppose that chronic exercise causes an unspecific adaptation, which might as well transfer to psychosocial or cognitive stressors as well ("cross-stressor adaptation hypothesis"). This article provides evidence that exercise entails all activation of the physiological stress regulation. Specifically, both neural (autonomic nervous system and sympatho-adrenal medullary system) and endocrine pathways (hypothalamic-pituitary-adrenal cortex) are activated. Moreover, trained individuals exhibit a reduced activation of these two regulation systems during exercise. However, this is only true if one looks at the absolute exercise intensity. Further, a high level of fitness results in an augmented reactivity under maximal exercise intensity. In turn, research provides only limited support for the validity of the cross-stressor adaptation hypothesis. Even though acute bouts of exercise lead to a reduced stress response when stressor tasks follow immediately, there is no evidence to conclude that chronic exercise training or aerobic fitness provoke a general adaptation effect. From a public health perspective, it is, however, remarkable, that trained individuals regenerate faster from non-exercise stressors. Finally, it is important to notice that the lack of a general relationship between exercise training and stress reactivity may be both due to substantial (i.e., specificity of the stress response) and methodological reasons (i.e., low intensity of the applied laboratory stressors).