# Good morning… let the stress begin. What is stress and how do we study it?

The American Psychological Association estimates that more than 70% of Americans regularly experience the physiological or psychological symptoms associated with chronic stress, with a third of the population thought to be living with extreme levels of stress. A pioneer of the study of stress as a biological phenomenon was the Canadian scientist Hans Selye, who considered stress as “the non-specific response of the body to any demand for change”. “Stress” has become a popular buzzword, and although many will experience and be aware of stress, this term is actually difficult to accurately define for a number of reasons: its subjective nature (everyone experiences stress differently, thresholds vary, etc.), the variable nature of the biological / psychological manifestation of stress and importantly, the inability to accurately, reliably and objectively measure stress. These and other reasons make it challenging to study stress both in laboratory animals and also in human subjects. We reviewed the strengths and limitations of various animal models of stress and contrasted the findings with stress responses in human subjects. It is important to emphasize that triggers for stress in humans such as marital/financial crisis, work related incidents, feeling of neglect, preparing for interviews/ examinations, etc. are often not possible to mimic in animals. Additionally, many animals will rapidly adapt to stress-inducing situations (acclimation) so that what used to be stressful initially will no longer elicit a satisfactory stress response, and that both humans and animals respond differently to acute versus chronic stress.

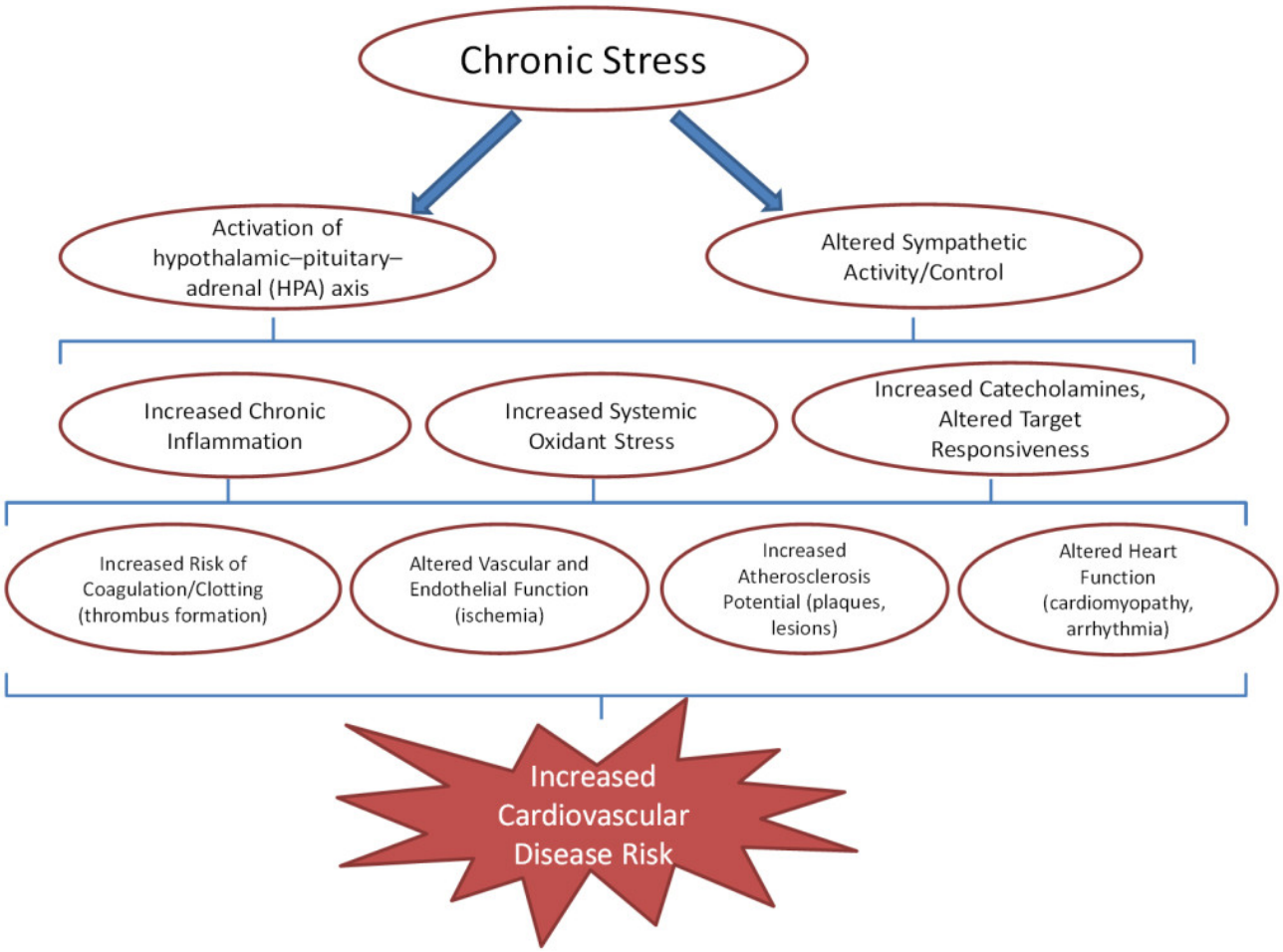


Fig. 1. Some mechanisms involved in stress-induced elevations in cardiovascular disease risk.

The stress response is a complex phenomenon (Fig 1) affecting virtually every organ in the body that is controlled by the nervous system, and is accompanied by increased chemical regulation by hormones (e.g. corticosteroids) released in the body. Our immune and inflammatory systems are also negatively impacted during periods of stress. We focused on animal models of stress and in particular, the effects on the cardiovascular system as the detrimental effects of stress on heart disease and blood pressure have been known for many years. Relatively recent data reports increased heart attacks during or after natural disasters and also in people with “type A” personalities. However, the mechanistic events linking stress to negative cardiovascular outcomes are poorly described although some consistent features are emerging. Critical to developing cardiovascular impairments and diseases related to chronic stress may be early damage to the endothelium of blood vessels, causing impairments to both vascular structure and vascular reactivity. Elevations in plasma levels of endogenous steroids and various inflammatory mediators are hallmarks of chronic stress.

| | Sunday | Monday | Tuesday | Wednesday | Thursday | Friday | Saturday |
|---|---|---|---|---|---|---|---|
| Stressor 1 | Alter Light/Dark | Social Stress (Cage Switch) | No bedding | Damp Bedding | Alter light/dark | Predator sounds (growling) | Predator Smells (Urine or Fur in cage) |
| Stressor 2 | Alter Light/Dark | Cage Tilt | Shallow Bath | Cage Tilt | Social Stress (Cage Switch) | Shallow Bath | No Stressor |

Tab. 1. Example week of stressors imposed on rodents for UCMS model

Studying stress in laboratory animals is challenging and many models are of an acute nature e.g. immersing rodents in low temperature water baths, immobilizing animals, combination of immobilization and cold temperature exposure, exposure to electrical shocks. These methods minimize the chronic psychological aspects of stress, however methods that incorporate elements of chronic stress include placing animals with aggressive “cage-mates”, removal of bedding or addition of excess water to their caging, isolating new born pups, exposure to predatory signals, abnormal noise levels or day-light signals (Table 1). When properly administered, this can create a chronic, unpredictable (i.e., unresolvable) level of exogenous stress on the animal, which does an excellent job of recapitulating numerous characteristics of human models of chronic stress, including altered neuroendocrine status, increased depressive responses to stimuli, etc. . Our opinion is that a model of chronic unpredictable mild stress that relies on constant changes in exposure to a variety of stressful stimuli would reduce habituation while at the same time producing all the changes (including circulating biomarkers) frequently occurring in humans.

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## Publication

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