

The Effect of Acute and Chronic Stress on Neurological and Biochemical Systems, and the
Protective Effect of Exercise on Stress System Degeneration and Dysfunction

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Introduction:

Stress is a phenomenon that permeates the existence of all organisms. In our society the word “stress” had connotations of “ability” or “toughness”, however from a physiological standpoint this grossly misrepresents stress and the role it plays in our lives. Stress is nothing more than a reaction to a “perceived stimulus that threatens to disrupt the homeostatic state of an organism”(Tsatsoulis et al. 2006, p.197). Yet this reaction cannot be viewed in a reductionist manner; rather it is a holistic effect that has its compromises and sacrifices. This has led to the idea of “allostasis” which is the adaptive response to homeostatic deviations, or “constancy through change” (Sapolsky, 1994, p. 9). The use of this stress response has its consequences. If it is overused or misused then it will start to accumulate “wear and tear”, leading to dysfunction and disease. This process of overuse is termed “allostatic load” (Korte et al. 2005). The mechanisms behind our response to stressors is extremely complex and nuanced, however it can be described in a simple metaphor; water is used by firemen to put out fires, but if they use too much water they could cause more damage in flooding than the original fire, or if they use the water inappropriately they may lose water-pressure and find themselves unable to extinguish the entire fire. In the same way the body responds to a stressful event with a specific response, if that response is too large then it could cause more damage than the initial stressor, or if that response is misappropriated then the body’s ability to deal with other events is diminished. Consequently disease develops and leads to death.

The purpose of this paper is to present an evidenced based review of the effect that acute and chronic stress has on an organism. For the sake of organization this will be

broken down into physical and mental components, but in the allostatic tradition it should be understood that these systems work in conjunction with each other, therefore their function and effect cannot be separated from one another. Lastly this paper will give support for the use of physical conditioning as a method for buffering allostatic load, and describe the explanations of this effect. The chronic or inappropriate activation of stress systems has been linked to numerous health disparities; including insulin resistance, visceral obesity, hypertension, dyslipidemia, all of which are precursors to metabolic and cardiovascular disease (Tsatsoulis et al. 2006). Chronic stress has also been associated with depression, anxiety, learned helplessness, and deficits on memory and cognitive function (Greenwood, 2008).

The Human Stress System:

The human stress system is composed of the hypothalamic-pituitary-adrenal (HPA) axis, and the sympathetic nervous system (SNS) (Tsatsoulis et al. 2006). These two systems work in coordination to mount a “fight or flight” response to a perceived threat. This response presents itself as; increased arterial pressure, a shift of blood away the viscera and into active muscles and the brain, increased rate of cellular metabolism, increased glycolysis, increased muscle strength, increased mental activation, and increased rate of blood coagulation (Guyton, 2006). The body mounts this response through the release of specialized neurotransmitters and hormones. The HPA axis is responsible for activating the release of glucocorticoids (GCs), of which 95% are in the form of cortisol (also known as hydrocortisone) from the adrenal cortex (Guyton, 2006). The effect of cortisol in the system is; mobilization of proteins from the muscles and fatty acids from adipose, increased

gluconeogenesis, which is the forming of carbohydrates out of proteins and fats in the liver, and an anti-inflammatory response (Guyton, 2006). The SNS is responsible for both direct sympathetic stimulation of organs, as well as indirect prolonged stimulation through activating the release of catecholamines from the adrenal medulla (Guyton, 2006) These hormones take the form of epinephrine and norepinephrine, which effect target organs in similar ways; increasing heart rate, inhibiting gastrointestinal function, dilating pupils, and other responses associated with sympathetic activation (Guyton, 2006). Both sympathetic and parasympathetic branches of the autonomic nervous system are continually active and operate at a basal rate called the sympathetic and parasympathetic tone, this concept is important when distinguishing the effects of an acute mass discharge of the HPA and SNS systems, compared to a chronic imbalance of sympathetic stimulation leading to degeneration and dysfunction.

The Effects of Stress on the Physical Body:

In a gross over-generalization, the effect of sympathetic activation is energy mobilization. This is useful in accomplishing a desired activity, which, in an evolutionary sense, is immediate survival. However, as noted above, stress is caused not only by the presence of a stressor, but the perception of the presence of a stressor. This subtle difference can be traced to as the root of the health disparities associated with a stressful life. In the presence of psychological stress, or perceived stress, the body reacts in the same manner as with physical stress, namely through the secretion of glucocorticoids and catecholamines (Ottoman et al. 1994). This prompts the effects described above, however in a case of psychological stress with the absence of a physical reaction, the energy

mobilized is not balanced out by increased oxidation, leading it to be placed back into storage (Ottoman et al. 1994). The level of insulin resistance and sensitivity in associated organs moderates this storage, yet in the presence of GCs, skeletal muscles become insulin resistant, insuring adequate glucose supply to the brain (Guyton, 2006). The only major option for energy storage is in adipose, which maintains its insulin sensitivity even in the presence of GCs (Ottoman et al. 1994). This adipose storage is mediated by glucocorticoid receptors, which are found more in visceral than peripheral fat deposits (Ottoman et al. 1994). It has also been found that GCs stimulate food intake, thus even further driving the organism into obesity, and specifically central obesity (Sapolsky, 1994). This central obesity leads to a cycle of metabolic dysfunction by secreting cytokines which further increase insulin resistance, leading eventually if unregulated to type 2 diabetes (Brinley, 1995). The presence of excess GCs also have a direct effect on circulating lipoproteins by decreasing the amount of LDL receptors on hepatocytes, prompting the liver to produce VLDLs and leading to hyperglyceridemia (Brinley, 1995). This high level of serum triglycerides, paired with the natural hypertension associated with sympathetic activation, further paired with oxidative damage, leads not only to atherosclerosis, but increased risk for stroke, heart attack, and cancer (Sapolsky, 1994).

Support for the causation of stress for cardiometabolic risk factors can be found in a 14 year longitudinal study of 10,000 civil servants called the Whitehall II study. This study was able to establish a dose-response relationship between exposure to stress and metabolic syndrome (Sapolsky, 1994).

The Effects of Stress on the Mind:

Stress has been linked to numerous physiological disorders including anxiety, depression, and memory loss (Sapolsky. 2000). This theoretically is linked to the hippocampus, a gyrus of the limbic system, having a high concentration of Glucocorticoid receptors making it more susceptible to the neurotoxic effects of GCs, and leading to dendritic atrophy and neural destruction (You et al. 2009). In rodent brains this effect has been linked to oxidative stress damaging the cascade that regulates glutamate and calcium (You et al. 2009). In rodent models it was also established that chronic stress increases nitrite levels and lipid peroxidation in the hippocampus leading to decreased spatial learning and memory (You et al. 2009). These studies have not been replicated in primate subjects and therefore lack external validity, however there are numerous case studies that point to similar mechanisms in human brains (Sapolsky 1996). Cushings syndrome is a pathology in which GC's are over produced as a result of a tumor in the HPA axis. This was not only correlated with hippocampal atrophy in a controlled study, it was also found that no atrophy occurred in the caudate nucleus, which has few GC receptors (Sapolsky, 1996). Similar results were found in depressive patients in which hippocampi volume decreasing an average of 14% (Sapolsky, 1996) The same is true of combat veterans suffering from Post Traumatic Stress Disorder, which found that longer duration of combat was associated with smaller hippocampi (Sapolsky, 1996). While these findings all point to similar conclusions, there are still problems establishing causation, due to a lack of understanding of the neural mechanism leading to these findings. The author of this study points out that should the research establish direct causation, it would have drastic effects on common

medical practices, particularly the use of cortisol to control numerous autoimmune and inflammatory diseases (Sapolsky, 1996).

The Buffering Effect of Exercise:

Much research has been done regarding the effect of physical inactivity on health status, and it is well understood that an “exercise-deficient phenotype” exists and is linked to cardio-metabolic risk factors (Greenwood, 2008). What the general population does not as well understand is the buffering effect that exercise has on allostatic load and the comorbidities associated with it. Multiple studies have shown that repeated exposure to physical activity improves glucose tolerance and insulin sensitivity, dyslipidemia, hypertension, and central obesity (Hawley, J.A. 2004). It has also been shown that physically active individuals have lower levels of triglycerides, LDLs, and higher levels of HDLs (Hawley, J.A. 2004). That paired with the finding that individuals with unfavorable lipid profiles respond positively to exercise training shows a therapeutic effect for physical activity. (Stewart. et al. 2005)

The mechanisms for this effect is due both to the structural and physiological changes associated with repeated exercise participation. Insulin sensitivity is increased due to increased muscle volume, increased blood flow to active muscles, and the increased capacity to oxidize fuels (Stewart. et al. 2005). The increased oxidative capacity due to mitochondrial biogenesis also has a positive effect on lipid homeostasis, leading to an increase in basal metabolism, thus balancing out the energy mobilized during sympathetic activation (Stewart. et al. 2005). It has also been argued that exercise assists in restoring

the natural genetic expression pattern designed to ensure survival during a stressful event, and the recovery from that event (Booth et al. 2002).

This buffering effect is further heightened by an increase in psychological and cognitive benefits associated with participation in an exercise program. Several studies have shown physical activity to reduce the incidence and severity of stress-related mood disorders, including anxiety and depression (Greenwood, 2008). These findings also show that the protective effect is consistent regardless of exercise type, for example aerobic versus anaerobic conditioning (Greenwood, 2008). This effect is associated with the increase of neurotransmitters, specifically serotonin and dopamine, as well as increased secretion of endogenous opioids, or endorphins (Greenwood, 2008). The protective effect of exercise against depression is so large that it has been found comparable to the protective effect of exercise for cardiovascular disease (Greenwood, 2008)..

Conclusion:

The body's response to stress is a tool that humans have used to survive and adapt to even the most inhospitable environments. Like most tools though, if it is misused to cause damage and lead to detriment. This misuse is characteristic of humanity and should be regarded as part of the learning curve as to how we are designed to function with-in our environment. While there is not need to promote a lifestyle with the absence of stress and disturbance, the use of recovery and conditioning to acclimate the system to alliostatic loads are essential in continuing our survival as a species and ensuring our quality of life.

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