Stress & the Brain: Introduction

Our bodies’ stress response results from a perceived threat in our environment. A stress response is coordinated by the hypothalamic-pituitary-adrenal (HPA) axis, which mediates cortisol release. Cortisol causes short-term physiological changes in our bodies during a fight or flight response. Therefore, cortisol in short bursts can be beneficial to our performance and survival. Chronic stress is a condition that results from dysregulation of the stress response system, causing inappropriate and long-term cortisol release. It is known that this chronic release of cortisol can damage many organs of our body, including the brain, which is the focus of this poster.

Stress & the Brain: Results

Chronic daily subcutaneous cortisol injections in rats significantly decreased neuronal proliferation in the prefrontal cortex (PFC) and in the molecular layer (ML) of the hippocampus. This task is known to rely on the medial temporal lobe memory system, which includes the dentate gyrus, a part of the hippocampus known for high levels of adult neuron proliferation.

Chronic daily subcutaneous cortisol injections in rats significantly decreased neuronal proliferation in the hippocampus and corpus callosum (BrdU staining).

Immobilization stress (immobilized by mesh and exposed to 1.5 cm-depth water for 1 hour) significantly decreased expression of BDNF mRNA and protein in the hippocampus 2 hours after stress.

Chronic dexamethasone (DEX) treatment in normal adult human subjects for four days (double blind) decreased ability in recall during a paragraph recall task (verbal declarative memory performance).

Stress & the Brain: Implications

The dentate gyrus is a part of the hippocampus known for high levels of adult neuron proliferation. Decreased proliferation in this area is linked to decreases in learning and memory. Since stress and glucocorticoids cause decreases in proliferation (Alonso 2000, Ekstrand et al., 2008), decreases in BDNF (Huang et al., 2005), and decreases in the number of synapses (Tata et al., 2006) in this area, stress is a likely cause of problems with memory and learning. This is supported by the finding that treatment with dexamethasone decreases verbal declarative memory performance in healthy adult humans (Newcomer et al., 1994). This task is known to rely on the medial temporal lobe memory system, which includes the hippocampus.

The hippocampus is also known to be involved in regulation of mood. Therefore, it makes sense that chronic glucocorticoid treatment has also been shown to increase depressive behaviors. If the hippocampus is being damaged by stress, this damage should affect its regulation of mood.

Exercise & the Brain: Introduction

Exercise has been found to have robust effects in offsetting the damaging effects of chronic stress in both young and old populations. While exercise can benefit many organs and tissues throughout the body, perhaps the most impressive exercise-modulated changes occur in the brain. Exercise can modulate the HPA stress mechanism and also ameliorate the destructive neurological effects of chronic stress. A sustained exercise regimen has been shown to enhance spatial learning and memory, facilitate neurogeneration, and offset neurological decline.

Exercise & the Brain: Experimental Results

The effect of exercise, stress, or both on BDNF mRNA

A two week long exercise regimen was shown to increase BDNF mRNA levels in chronic unpredictable stress (CNS) condition mice.

Exercise increases brain-derived neurotrophic factor (BDNF) protein expression

BDNF protein expression is significantly upregulated in rats undergoing moderate levels of exercise (E) compared to the sedentary control (C) group. It is believed that norepinephrine release during exercise may activate BDNF expression at the transcriptional level, thus resulting in higher protein expression.

Exercise increases dentate gyrus cerebral blood volume (CBV) in mice. CBV is correlated with neurogenesis in the mouse hippocampus, indicating that exercise-induced increased blood supply to certain regions of the brain can cause amplified neurogenesis.

Regular exercise significantly increases neurogenesis

BrdU+ is a measure of cell proliferation and neurogenesis in the brain. BrdU+ cells are significantly (about 4-fold) more prevalent in the ‘runner’ rats than in sedentary.

Exercise increases blood flow to the brain, thus providing oxygen and nutrients that are necessary to protect the brain against age- and disease-related cognitive decline.