

Revathi Kaduru

August 9, 2014

Yale University Research Publication

Stress-Related Mental Diseases

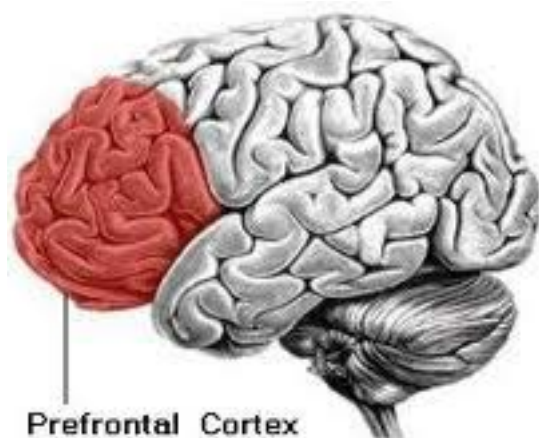
Abstract:

This past summer, I was granted the opportunity to work with Dr. Duman and the post-doctorate researchers at the Ribicoff Labs located at Yale University where they research in the topics of molecular psychiatry and neuroscience. Psychiatry and neuroscience are both interconnected and the main focus of these topics is surrounded around the brain. Psychiatry is the study of mental illnesses, emotional disturbance, and abnormal behavior, and neuroscience deals with the structure or function of the nervous system and brain. I was fortunate enough to have worked with two post-doctorate researchers, Tina Franklin and Sophie Dutheil, who allowed me to assist them with their research and experiments and taught me new scientific information that is associated with their experiments. This paper discusses my personal experience working in the research field and also about the experiments and scientific knowledge that I gained from this experience. The hypothesis that was made was that increased levels of cortisol in the blood caused by stress can lead to mental diseases such as major depressive disorder, anxiety, and post-traumatic stress disorder.

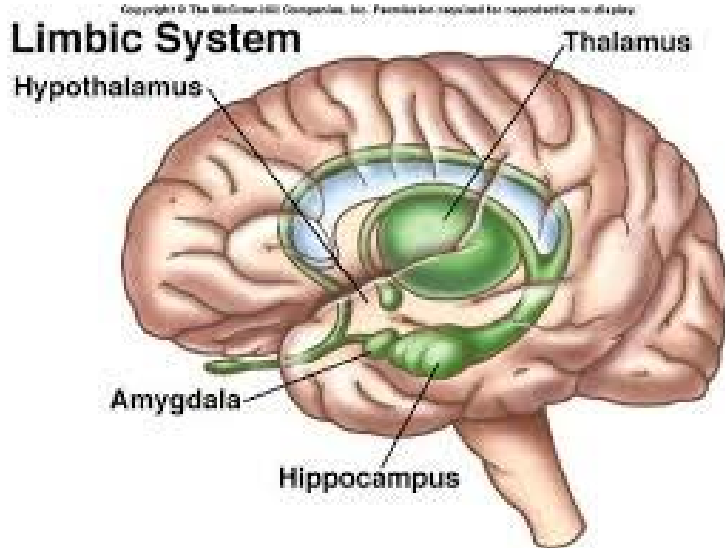
Structure and Function of the Brain:

The brain is an organ that serves as the center of the nervous system in all vertebrate and invertebrate that function as the coordinating center of sensation and

intellectual and nervous activity. The central nervous system consists of the brain and the spinal cord and the peripheral nervous system consists of the nerves. The cerebrum or cortex is the largest part of the human brain and is associated with higher brain function such as thought or action. The prefrontal cortex is the gray matter of the anterior part of the frontal lobe that is highly developed in humans and plays a role in the regulation of complex cognitive, emotional, and behavioral functioning, suspected to play an important role in cognitive control. The limbic system consists of the following structures: thalamus, hypothalamus, amygdala, and hippocampus, and is often referred to as the “emotional brain”. The hippocampus is part of the temporal lobe and is involved in learning and memory process. The hippocampus is also important for converting short-term memory to more permanent memory, and for recalling spatial relationships in the world. As you can see, there are many complex components that make up the brain and each part is involved in making sure that the brain and the rest of the nervous system functions properly.



The Limbic System

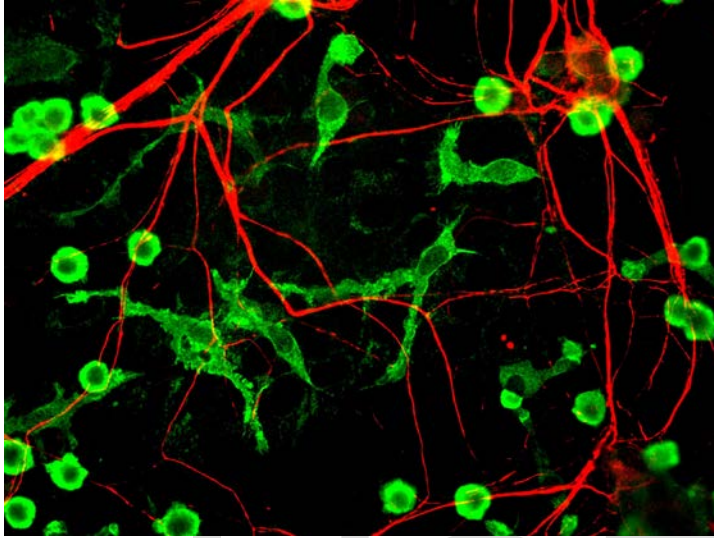


Microglia and Astrocytes

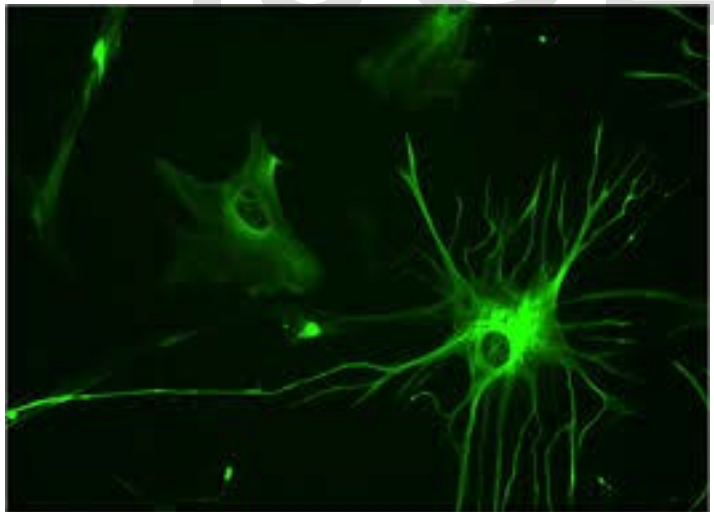
The glial cells are the non-neuronal cells of the central nervous system and play a crucial role in the development and maintenance of the neurons that they support.

Microglia is the type of neuronal support cell that are found in the central nervous system of invertebrate and vertebrate that functions primarily as an immune cell. These cells mediate immune response in the central nervous system. Astrocytes are the most numerous and diverse neurological cells in the central nervous system. Astrocytes create the brain environment, build up the micro-architecture of the brain parenchyma, maintain brain homeostasis, and control the development of neural cells. Also, during inflammation and injury, they divide and wall off damaged areas. The main importance of microglia is that it acts as the first and main form of active immune defense in the central nervous system.

Microglia



Astrocytes

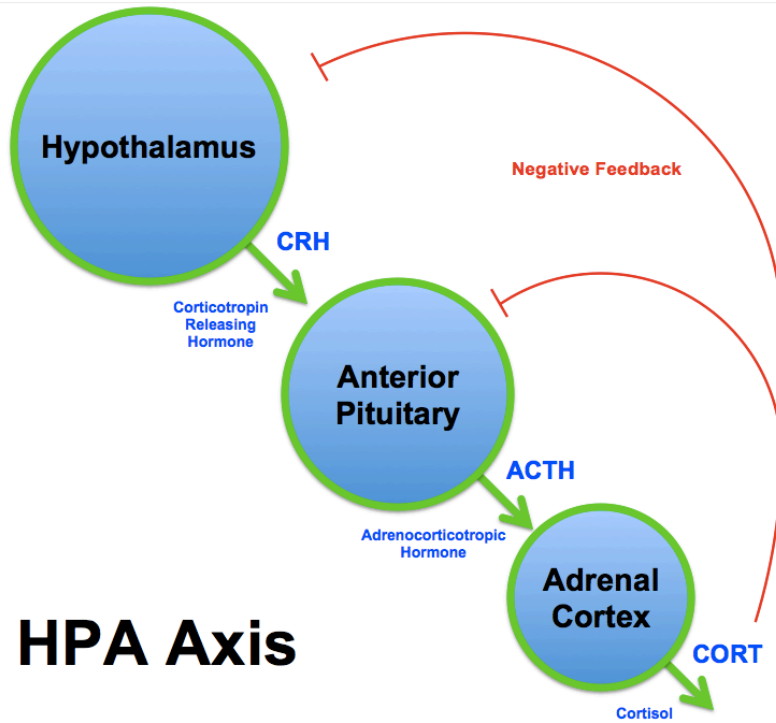


What is Stress?

Stress is something every human faces in his or her everyday life, but what really is stress? Stress is defined as a state of real or perceived threat to homeostasis. Stress triggers many physiological and behavioral responses, known as a stress response. The maintenance of homeostasis in the presence of stressors requires the activation of several responses such as the endocrine, nervous, and immune systems.

Cortisol and the HPA Axis

Cortisol is known as the stress hormone and just happens to be the public health enemy. Elevated cortisol levels have been shown to interfere with learning and memory, lower immune function and bone density, increase weight gain, blood pressure, cholesterol, and heart disease. Chronic stress and elevated cortisol levels also increase risk for depression, mental illnesses, and lower life expectancy. Cortisol is released in response to fear or stress by the adrenal glands as part of the fight-or-flight mechanism. The hypothalamic-pituitary-axis is a complex set of interactions between the hypothalamus, the pituitary gland, and the adrenal or suprarenal glands. The HPA axis helps regulate temperature, digestion, immune system, mood, sexuality, and energy usage. It is also a major part of the system that controls reactions to stress, trauma, and injury. The HPA axis is involved in mental illnesses such as anxiety, bipolar disorder, post-traumatic stress disorder, and major depressive disorder.



HPA Axis

Cytokines

Cytokines are types of proteins produced by the cells and they interact with the cells of the immune system in order to regulate the body's response to diseases and infections. There are two main types of cytokines: pro-inflammatory and anti-inflammatory. Some cytokines act to make diseases worse (pro-inflammatory), whereas others serve to reduce inflammation (anti-inflammatory). One cytokine is known as IL1 β and the protein encoded by this gene is a member of the interleukin 1 cytokine family. This cytokine is an important mediator of the inflammatory response, and is involved in cell proliferation, differentiation, and apoptosis. Another cytokine is TNF α , which is a pleiotropic inflammatory cytokine.

Main Focus of Research:

Stress is a common occurrence in everyday life and chronic or traumatic stress can be a hastening factor for illnesses related to that of the central nervous system. The goal of this research that I was assisting on was to determine how increased levels of stress could lead to mental illnesses such as anxiety, depression, and post-traumatic stress disorder. In order to test this statement, there was a set of control animals and a set of chronic unpredicted stress animals. The animals that are used are rats. The chronic unpredicted stress (CUS) animals are separated from the control animals and are placed in a behavioral room and each day two different stressors are given to the animals. The different stressors involve rotation, restraint, swim, food/water deprivation, isolation, light off/light on, wet bedding, crowding, and cold. Rotation is when the animals are placed into two cages of at least six in each one and are placed on a rotator for an hour long. The restraint stress test is when the CUS animals are placed in tubes that constrict them from moving and they are placed in the tubes for an hour long. The swim stressor is when the animals are placed in water tanks and made to swim for ten minutes. The food/water deprivation is when the animals are lacking food and water for almost twelve hours. Rats are more comfortable when they are placed in pairs in the cages as they feel as though they have a companion. Isolation stressor is when the animals are placed in mice cages by themselves for up to twelve hours. These different stressors are given over a period of around 28 days. The effect of CUS in these animals is determined by behavioral tests such as Forced Swim Test (FST) and Sucrose Preference Test (SPT). As mentioned before, cortisol is the main stress hormone and it is released in response to

stress and a low level of blood glucocorticoid. In addition to the behavioral changes in these animals, cortisol levels will also be tested.

Forced Swim Test



Conclusion

Throughout this research experience, I was able to gather a vast amount of information in molecular neurobiology, psychiatry, animal handling and stressors, and lab techniques. The seven weeks that I spent at Yale University was an experience that helped not only to excel and expand my knowledge in the science field, but also helped open my eyes in the direction of my future career path. Stress affects the majority of the population on a daily basis and can cause many behavioral changes that affect the way a

person functions. Further research is being conducted on how increased stress levels can lead to various mental diseases that affect many people on a daily basis.

IJSER