Stress and Its Effects on the Brain and Body

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Stress is a broad term that can be used to describe various demands and the consequential physiological responses of the body. The word stress can sometimes refer to experiences that are beneficial in one's life and that lead to personal growth such as having a baby or moving in with a spouse. Oftentimes however, the word stress is used to refer to negative experiences such as going through a divorce, financial difficulties, or working overtime; and sometimes stress can be caused by traumatic events such as war, assault, or natural disasters. Depending on the source of stress, if the stressor is real or perceived, or whether the stressor is physical or psychological, such stressors have distinct physiological responses on the brain and body that are ultimately attempts to process the stress and re-establish homeostasis. The central nervous system and the autonomic nervous system activate different mechanisms during stressors, such as the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic-adreno-medullar (SAM) axis, which serve different functions for the body in response to threat. In addition, many brain structures are involved in the stress response such as the prefrontal cortex, the amygdala, and the hippocampus. While some individuals have life experiences, support systems, neurobiological functioning and genetics that support brain functioning that is capable of adapting to stressors and restoring homeostasis, many individuals do not have this same ability to cope with stress, causing maladaptive responses such as psychiatric conditions, addiction, immune dysfunction or endocrine disorders. This paper examines the neurobiological mechanisms associated with stress and its acute and chronic physiological effects on the brain and body.

The Stress Response and the SAM Axis

Hans Selye, a European-Canadian endocrinologist, was the first person to introduce the concept of stress in 1936. Selye's theory described the body's response to physical, environmental, or psychological stress in three consecutive stages: the alarm stage, the resistance stage, and finally the stage of exhaustion. The initial alarm stage is when the body's defence mechanisms are heightened, preparing for defence, or "fight-or-flight" responses. This first stage activates the sympathetic nervous system and is meant to last for only a brief time, after which the second stage of resistance engages. The resistance stage is when the body is still staying alert but its defence mechanisms begin to relax as it attempts to adapt to the stressor and regain homeostasis. After prolonged stress, the third stage of exhaustion begins, in which the body experiences a deceleration of its functions because it no longer has the energy to maintain it's heightened state. As mentioned above, the alarm stage activates the body's sympathetic nervous system, a subdivision of the autonomic nervous system that is responsible for readying the body for immediate danger. When the sympathetic nervous system is activated, the sympathetic-adreno-medullar (SAM) axis engages which causes the adrenal, medullar, and sympathetic nerves to release epinephrine into the body. Due to epinephrine and norepinephrine being released into the body, the SAM axis provides an immediate physiological response that increases heart rate, increases blood pressure and suppresses digestive functioning. Functionally, the SAM axis increases alertness, sharpens awareness of the environment and creates a defensive stance of the body, readying it for attack. The paraventricular nucleus of the hypothalamus, the locus coeruleus of the pons, and the rostral ventrolateral medulla provide neural output through sympathetic neurons which cause the physiological arousal associated with the SAM axis. The physiological response of the body in the alarm stage has evolved to help humans survive

immediate adverse experiences. While highly adaptive, it is only meant to be activated for a short period of time until the threat subsides and the body can return to normal and balanced functioning. If however, the threat persists, the body will move into the resistance stage, activating a slower hormonal mechanism that allows for a longer lasting responses of the body.

The HPA Axis

If the body experiences longer-lasting stress, whether physical or psychological, the body moves into the second stage of the stress response in which the hypothalamus becomes activated, including the paraventricular nucleus, which generates the activation of the hypothalamic-pituitary-adrenal (HPA) axis. The paraventricular nucleus creates oxytocin, vasopressin and corticotrophin-releasing hormone which are all secreted to, and stored in the posterior pituitary gland. When corticotrophin-releasing hormone arrives at the anterior pituitary gland, adrenocorticotropic hormone (ACTH) is released which enables the adrenal cortex to release cortisol into the body. Cortisol can compromise the immune system, effect cognitive abilities, increase glucose availability in the bloodstream, inhibit reproductive activity, alter metabolic functioning and effect many other systems that encourage physiological and behavioural changes. Cortisol is also responsible for providing negative feedback to the pituitary and hypothalamus to inhibit further HPA activation which helps the body become accustomed to stressors that are not life-threatening, to conserve energy and resources and encourages habituation of the HPA axis. Habituation occurs when the body's response to a certain stressor decreases with continued exposure to that stressor. The HPA axis has been shown to habituate primarily to psychological stressors, which include limbic brain activity, and not as readily to physical or physiological stressors, which do not significantly involve the limbic brain. Habituation has been studied in humans who repeatedly perform parachute jumps out of

airplanes; their HPA axes responding less with each progressive parachute jump. Similar to the SAM axis, the HPA axis is meant to help the body adapt to stress and survive however, when this system runs on overdrive or it is not able to habituate due to factors that will be discussed below, this can lead to psychiatric conditions such as anxiety, depression, post-traumatic stress disorder, or addiction.

Chronic Stress, Early Life Adversity, Psychiatric Disorders, and Addiction

If the body is not able to adapt to its present stressors, it enters the third stage in the stress response, exhaustion, in which the body begins shutting down in order to preserve its resources. The inability of an individual to habituate to stress can be due to many reasons such as: chronic stress, intensity of the stress, early life adversity, genetic makeup, or behavioural and environmental factors. When an individual is unable to habituate, this can cause feelings of "distress" where they feel ineffective against managing the stressor, causing exhaustion of the physiology and psychological coping mechanisms. Chronic stressors are ones that are constantly provoking us at low levels which can lead to anxiety, insomnia, excessive eating, substance use, or isolation from friends and family. Under chronic stress, the neurochemistry of the brain can begin to change. For example, the dendrites in the amygdala, hippocampus and prefrontal cortex begin to shrink which can lead to social avoidance, cognitive rigidity, anxiety and post traumatic stress-type behaviours. Additionally, the cortical neurons located in the frontal lobe expand, which can cause hyper-awareness of one's surroundings. In addition to chronic stress, early life adversity, such as poverty, abuse, lack of nurturing, or unstable family environment have been shown to have effects on brain development which are associated with future maladaptive coping behaviours such as alcoholism, drug addiction, and risk-taking behaviours. These early life experiences have been shown to have a direct effect on the proper functioning of the HPA axis'

negative feedback loop, a decrease in communication between the prefrontal cortex and reward centres in the brain, and modifications in the hypothalamus, brain stem, amygdala, and hippocampus. This impaired functioning can lead to an individual's inability to innately regulate their stress response, which often leads to the individual attempting to regulate themselves by other means (i.e., the use of substances). In studies where rats were subjected to stressors during the prenatal period of development, such as lack of nurturing or inadequate maternal care, it was shown that their hippocampal development was impaired, their amygdala was underdeveloped and the presence of corticosterone (cortisol in humans) in their systems had adverse effects. Because of the dysfunction that can develop in HPA axis functioning, adverse early life experiences are often correlated with the development of psychiatric disorders later in life. While chronic stress, early life adversity and psychiatric disorders are all interconnected with the stress response, affecting HPA axis and brain functioning, stress also elicits cognitive responses that have different effects on many parts of the brain. This paper will primarily examine the role of the prefrontal cortex, the amygdala, and the hippocampus in the stress response.

The Prefrontal Cortex, the Amygdala, and the Hippocampus

Stressful experiences have significant effects on the prefrontal cortex, amygdala, and hippocampus which together, effect cognitive, emotional, neuroendocrine, and autonomic functioning. The prefrontal cortex plays a role in movement, working memory, cognitive control, emotional reactivity, goal execution, and decision making. It is also important for developing appropriate behaviour in response to specific environments and the ability to modify or inhibit that behaviour as needed. The prefrontal cortex sends signals to many brain regions but specifically, the signals it sends to the amygdala and the brain stem help regulate the autonomic nervous system, neuroendocrine systems, and the HPA axis. The prefrontal cortex is vulnerable

to damage as a result of stress and its cognitive abilities can become highly impaired depending on the type and duration of the stressor. In studies with rats, short-lasting stress strengthened the number of synapses as well a synaptic activity within the prefrontal cortex while longer-lasting stress lasting up to seven days impaired memory recognition, a function controlled by the prefrontal cortex. Repeated, chronic stress lasting for 21 days or longer caused functional and structural alterations in the prefrontal cortex such as spine loss and dendrite shrinkage of the neurons. Short exposure to stressors can temporarily improve prefrontal cortex functioning however, long-lasting and chronic stress begin impairing prefrontal cortex functioning including memory, clear thinking and reasoning, emotional regulation and rational decision making.

The amygdala is a brain structure that is central in regulating and anticipating emotional information. The basolateral nucleus of the amygdala is especially prominent in processing psychological stress, becoming most activate during anticipatory stress. Neurons in this area of the amygdala have also shown an increase in their activity after emotional stress which may play a role in solidifying memories in regards to stressful experiences which functionally, would enable people to remember what experiences to avoid in the future but can also lead to anxiety-like behaviour. Human and animal studies have shown the amygdala can become hyperactive in the presence of stress while a simultaneous reduction of the inhibitory neurotransmitter gamma-aminobutryic acid (GABA) occurs. GABA works as one of the main inhibitors in the nervous system and when the amygdala is at rest, GABA produces a high level of inhibition which allows the body to remain fairly regulated in the presence of moderate stressors. During longer-lasting stress, more severe stress, or traumatic events, this inhibition is removed, leading to hyper-reactive states. These hyper-reactive states of the amygdala are often seen in patients with generalized anxiety, mood disorders, depression, post-traumatic stress disorder, and

schizophrenia. However, according to Zhang (2018), it is not clear whether the loss of GABA inhibition is the cause of these psychiatric disorders or the psychiatric disorders cause the loss of GABA inhibition. The amygdala is very functional for our survival in scenarios with acute, short-duration stressors however, longer-lasting and chronic stressors appear to have negative implications on the body's physiological and psychological functioning.

The hippocampus, located in the medial temporal lobe is responsible for cognitive functions such as memory formation, learning, and emotional regulation. In recent studies, it has been shown that the hippocampus may be very vulnerable to stress as it contains a large number of cortisol receptors. These studies suggest that exposure to stress and the subsequent elevation of cortisol levels can impair hippocampal functioning, worsening memory task performances. This can lead to a type of impaired learning called "learned helplessness" in which a person believes that their behaviour will have no effect on the stressor. This belief is followed by significant changes in an individuals ability to learn in the future due to their inability to take action. According to Kim et al. (2015), learned helplessness was first observed in dogs in the 1960s when they were exposed to shocks that they could not escape from and subsequently, stopped trying to escape. Long-lasting and traumatic stressors can also cause structural changes in the hippocampus such as a reduction in its volume which has been seen in patients with PTSD as well as rats who were subjected to chronic restraint. Chronic stress can also cause structural changes in the dendrites of the neurons in the hippocampus, causing a reduction in cells. These structural changes can impact an individual's verbal recalling of events, spatial navigation, and memory of past personal experiences. While the hippocampus is vulnerable to stress, it also plays a major role in the regulation of stress, as it helps with the negative feedback system of the HPA axis. The prefrontal cortex, amygdala, and hippocampus are all connected and affect each

other's functioning. For example, the amygdala is important for detecting potential danger while the hippocampus provides environmental information about the potential danger; therefore, processing emotional information in context with the situation is dependent on the amygdala and hippocampus interacting with each other. The prefrontal cortex is able to make associations between the environmental information and the potential danger; therefore extinguishing fear is dependent on the prefrontal cortex interacting with the amygdala. While many more are involved, the prefrontal cortex, amygdala and hippocampus are three of the main brain structures involved in the stress response. In addition to the central nervous system and autonomic nervous system, stress has a large impact on the immune system and other bodily systems.

Stress, The Immune System, and Other Effects on the Body

Many studies have found a connection between the stress response and its impact on our physical health and immune system functioning, increasing our susceptibility to illness and disease. Stress has been shown to activate the immune system in order to help defend the body against possible physical wounds and subsequent infections and has also been shown to suppress the immune system in the presence of chronic stress. Acute, short-term stressors have been shown to increase levels of cytokines in the body, which produce inflammatory responses in the body. The prefrontal cortex, amygdala and hippocampus become inflamed particularly due to social stressors, whereas the hypothalamus becomes inflamed due to physical stressors. Chronic inflammation in the body has been linked to diseases such as heart disease, rheumatoid arthritis, inflammatory bowel disease and Alzheimer's disease. Inflammation is also seen in higher rates in people who suffer from depression. Marinova (2023) examined the physical symptoms associated with psychiatric disorders including abnormal blood oxygen levels that have been found in patients with generalized anxiety disorder affecting the amygdala, prefrontal cortex,

hippocampus and insula, and a reduction in bone mineral density in patients with extreme childhood stress. In addition, specific emotional states have also been linked to certain physical ailments. For example, anger, depression, and anxiety have been shown to increase the risk for health declining behaviours such as smoking, insomnia, poor eating and exercise choices which all increase the risk for cardiovascular disease. While the stress response is an intelligent mechanism of the body, we can see that if it is chronically activated or has been impaired due to adverse experiences, it can cause a wide range of undesirable physical and psychological effects. Learning how to build resilience and manage stressors could be imperative for creating healthy functioning individual.

Stress Resilience and Reduction Practices

Managing stress can be both a personal responsibility as well as a societal responsibility. On a societal level, government policies could be altered to help lower stress levels, especially in those with lower socioeconomic status. McEwen (2017) suggests that government policies are synonymous with health policies and that creating accessible community services that enable individuals to develop beneficial lifestyle practices should be essential. On a personal level, individuals can help themselves by developing practices that create resilience and lower the stress response which include practices that help parasympathetic mechanisms engage, help reduce inflammation in the body, and practices that encourage a healthy functioning body. In contrast to the sympathetic nervous system, the parasympathetic system helps the body rest, relax and digest properly. Practices such as meditation, breathing exercises, walks in nature, time in healthy social situations, or going to therapy would all help parasympathetic functioning engage and support the body in creating homeostasis. Practices that encourage a healthy functioning body include regular moderate physical activity, a healthy diet, and supplementation

to reduce inflammation such as probiotics or omega three fatty acids. Developing resilience includes the intentional dysregulation of the body in order to practice calming the system immediately afterwards. For example, Rybnikova et al. (2022) reviewed the adaptive effects of hypoxic training (training in environments with reduced oxygen) on the brain and body and found immense benefits for a variety of dysfunctions including cardiovascular and cerebrovascular diseases. In addition to its effects on such diseases, Rybnikova et al. (2022) suggest that hypoxic training can be used in healthy individuals to help improve autonomic functioning which leads to increased resiliency and tolerance to stress. While personal responsibility is a major factor in stress reduction, there are many societal and familial factors such as genetics and generational trauma which would require a much larger intervention in order to help prevent stress and stress related disorders. It is also important to note that normal hormonal fluctuations that are seen in women who experience menstrual cycles, pregnancy, or menopause, can also affect individual's ability to manage and cope with stressors.

Conclusion

While stress is a broad term that is used by individuals to describe a general feeling, we now know that what people are referring to is a specific series of physiological and psychological functioning. Stressors, which have the potential to cause the stress response, exist on a vast spectrum of experiences that can range from something such as going to get groceries to something such as a traumatic experience at war. Based on neurobiological, genetic, and/or experiential life factors, each individual will react to stressors differently and possess different levels of innate stress resilience. The SAM axis is essential for the survival of acute dangerous situations, while the HPA axis is essential for helping the body function under longer-lasting stressful conditions. When these systems are not functioning properly, or are in chronic overuse,

this can lead to short-term and long-term issues that involve many different brain structures, particularly the prefrontal cortex, amygdala, and hippocampus, and can lead to adverse experiences such as addiction, neuropsychiatric disorders, or physical illness. The highly adaptive neurobiological mechanisms of acute and chronic stressors involve many different segments of the brain and body working together to regulate learning, memories and decision making. The stress response is however, maladaptive in instances when stressors create too much of a demand for the brain and body to cope with. In either case, individuals are generally capable of adjusting their environments and coping mechanisms in order to help the stress response and all systems involved to function optimally. The neurobiological mechanisms associated with acute and chronic stress have vast physiological and psychological effects on the brain and body which can be highly adaptive for our survival but under certain circumstances, have been shown to become maladaptive.

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