The impact of stress on development and cognition: Effects across the lifespan

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I Abstract

Stress is a response to adverse circumstances that creates tension and emotional strain within the individual. There are two types of stress: chronic (a consistent apprehension toward a situation) and acute (a discrete response toward an adverse situation). Stress triggers the activation of the hypothalamus-pituitary-adrenal (HPA) axis, culminating in the production of glucocorticoids by the adrenals. They can act as transcription factors and so regulate gene expression. Thus, glucocorticoids can have long-lasting effects on the functioning of the brain regions that regulate their release.

In young children and early adolescents, stress reduces the volume of the hippocampus, and hence it negatively modulates the development of brain structures compared to healthy controls. Additionally, stress has been shown to adversely affect cognitive performance in test achievements and applies to tasks beyond educational administered tests.

In adults, stress impairs memory due to increased hippocampus function. In addition, stress is known for enhancing fearful memory, thus creating an abnormal fearful state. Furthermore, it causes changes in the dendrites and takes ten days to regulate them. It also impairs spatial learning and can be reversed 21 days later. The effects of chronic stress in adulthood are reversible, whereas, for infants, it is permanent.

Keywords: Stress, Development, Cognition, Chronic stress, Acute stress, Hippocampus, Memory, Pregnancy.

II Introduction

Stress is the body's response to physical, mental, or emotional pressure. Stress causes chemical changes in the body, raising blood pressure, heart rate, and blood sugar levels 7. During acute stress, an individual will generally develop a short physiological response to the presented stressor, while chronic stress exposure will elicit a sustained maladaptive psychological response 16. Additionally, unlike acute stress, where the initial response to the stressor is phasic, an individual who experiences chronic stress is generally exposed to the stressor over an extended period 5.

Clinical and basic science research has provided strong evidence that prolonged exposure to psychological stress can lead to behavioral deficits and psychiatric illnesses, specifically depression and anxiety 8. Additionally, elevated stress has been linked to other psychiatric disease states, such as depression, anxiety, and obsessive-compulsive disorder (OCD)27. Regarding systemic disorders, meaning people who suffer from bodily illnesses, such as heart failure, cancer, diabetes, and obesity, sufferers also experience elevated levels of

stress28. Thus, it can be concluded that stress could be a powerful driver for developing these diseases 26. Exposure to chronic stress increases the risk of hypertension 29, heart attack, or stroke 16. Specifically, when an individual experiences repeated acute and persistent chronic stress, it can contribute to inflammation in the circulatory system. After prolonged stress, whether acute or chronic, the coronary veins (arteriole receiving deoxygenated blood from the heart, the heart can collapse 20), increasing an individual's chance of having a stroke or heart attack 10. This can put an individual at increased risk for a variety of physical and mental health problems, including anxiety, depression, digestive issues 17, headaches 18, muscle tension 10, heart disease20,21, heart attack 20,21, high blood pressure 22, sleep problems 23, weight gain10, and memory and concentration impairment 11.

Cortisol is a steroid hormone in the glucocorticoid class of hormones, 30. When used as a medication, it is known as hydrocortisone 31. It is produced in many animals, mainly by the zona fasciculate of the adrenal cortex in the adrenal gland 32. It is produced in other tissues in lower quantities, 12,10, such as the liver, skin, and adipose tissue, and can also produce cortisol in smaller amounts33. This review article aims to inform and raise awareness of the effects of stress on the human body through the different stages of development.

III Body

Chronic versus Acute Stress

Chronic and acute stress have different effects and connotations on the body. Chronic stress impairs memory because of decreased hippocampal function 35. The hippocampus is involved in memory formation, and chronic stress has been shown to affect this region of the brain 34. Stress hormones, such as cortisol, can have a toxic effect on the hippocampus, leading to impaired spatial and declarative memory (36- 34). Acute stress is pervasive and can profoundly influence cognitive functions. One critical function modulated by stress is cognitive flexibility, which refers to adapting behaviorally to situational demands 37. It also regulates the functioning of mechanisms such as the immune system 39 and cardiovascular system 38 and helps maintain homeostasis 4. A threat stimulus triggers a fear response in the amygdala 40, a known node for intergrading associative fear cues 41. After the amygdala detects the sensory threat cues, it activates downstream areas in preparation for motor functions involved in fight or flight (42- 43- 44). In addition, threatening cues are perceived as stressful (Figure 1 A), and thus, triggers the release of stress hormones, such as cortisol and adrenaline (Figure 1 B), and activates the sympathetic nervous system 45 46.

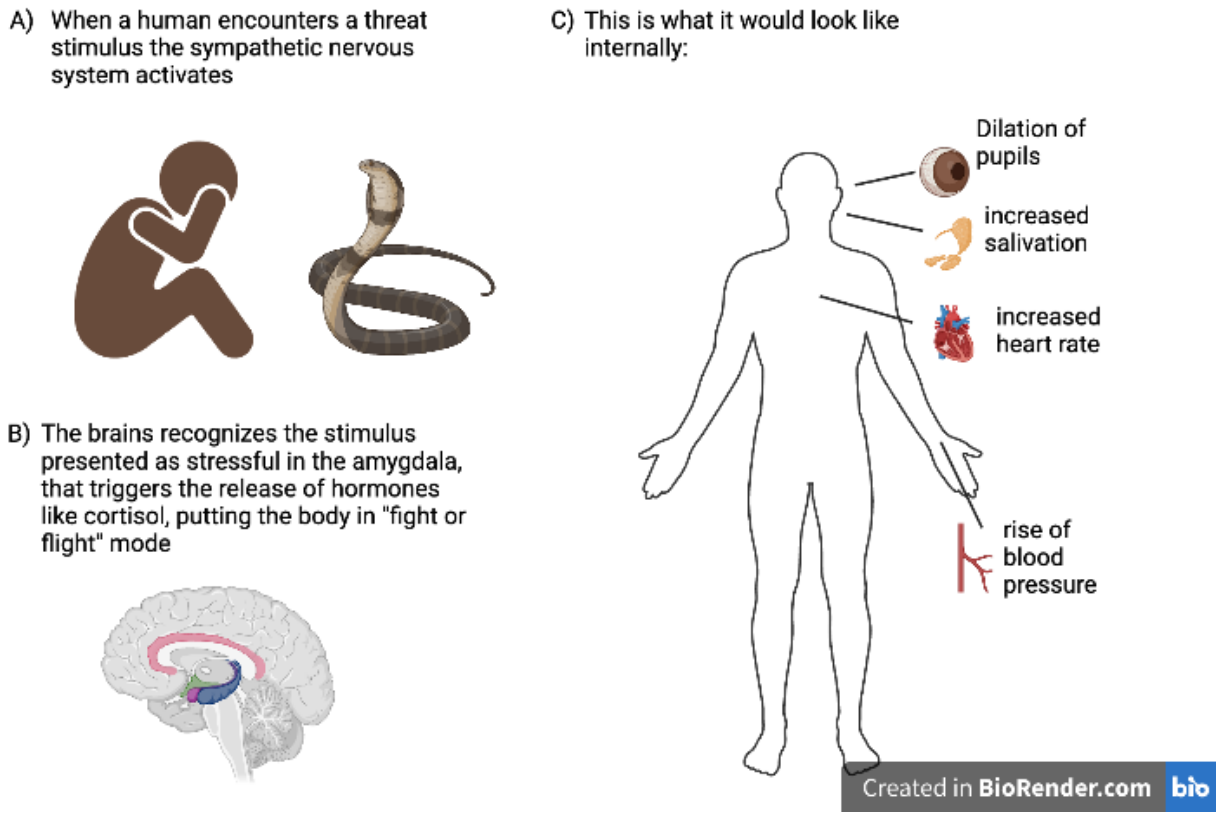

Figure 1. The image above shows what happens to the human body while they go through stress. (A) Shows an individual crowd over in visible distress next to a cobra snake, this is evidentially a stressful citation and thus, the sympathetic nervous system activates. (B) Shows the areas of the brain triggered by the stressful situation, activating the “fight of flight” mode. The colored areas are hypothalamus, hippocampus, amygdala. (C)Shows a human body and the sequences of changes that the body undergoes when the sympathetic nervous system is active. All panels in the figure were created with BioRender

This leads to bodily changes that prepare us to be more efficient in danger: The brain becomes hyperalert 51, pupils dilate 50, the bronchi dilate 10, breathing accelerates 48, heart rate and blood pressure rise (Figure 1 C) 47 48. The skeletal muscles experience increased blood flow and a surge of glucose. Meanwhile, non-essential organs like the gastrointestinal system undergo a deceleration in their activity levels 15.

In Utero and childhood consequences of stress exposure

Any stress has consequences on the prenatal stage of development. It alters the baby's dopaminergic system, 1 58, which is involved in reward- or drug-seeking behavior, and they become more susceptible to acquiring addictive behaviors 55. Stress during pregnancy is also linked to lower weight and size 57 in the baby, and it manifests its effects through the child's developmental stages 56,1. A single or repeated exposure to stress affects the hypothalamic-pituitary-adrenal (HPA) axis. (24), It passes to the placenta, affects the baby's serotonin levels, and modifies development 59,1.(Figure 2 A) Glucocorticoids are essential for

normal brain maturation: they initiate terminal maturation, remodel axons and dendrites and affect cell survival. It alternates neural structure 60,61. Cortisol is known to cross the placenta and consequently influence various aspects of development in the human fetus 2,62. The effects of elevated cortisol levels on the fetus may vary from defective development to spontaneous abortion 2. The first trimester is characterized by rapid organ development 63. Therefore, stress exposure in this period leads to widespread, global effects like cognitive dysfunction 64, heart malformation, 66 cataracts, 49 deafness 43, and genital and intestinal abnormalities 2.(Figure 2 A) In the second and third trimesters, the organs mainly enlarge and undergo refinement 19. Stress exposure in this period leads to low birth weight, skeletal abnormalities, and hearing loss 2 65. (Figure 2 B)

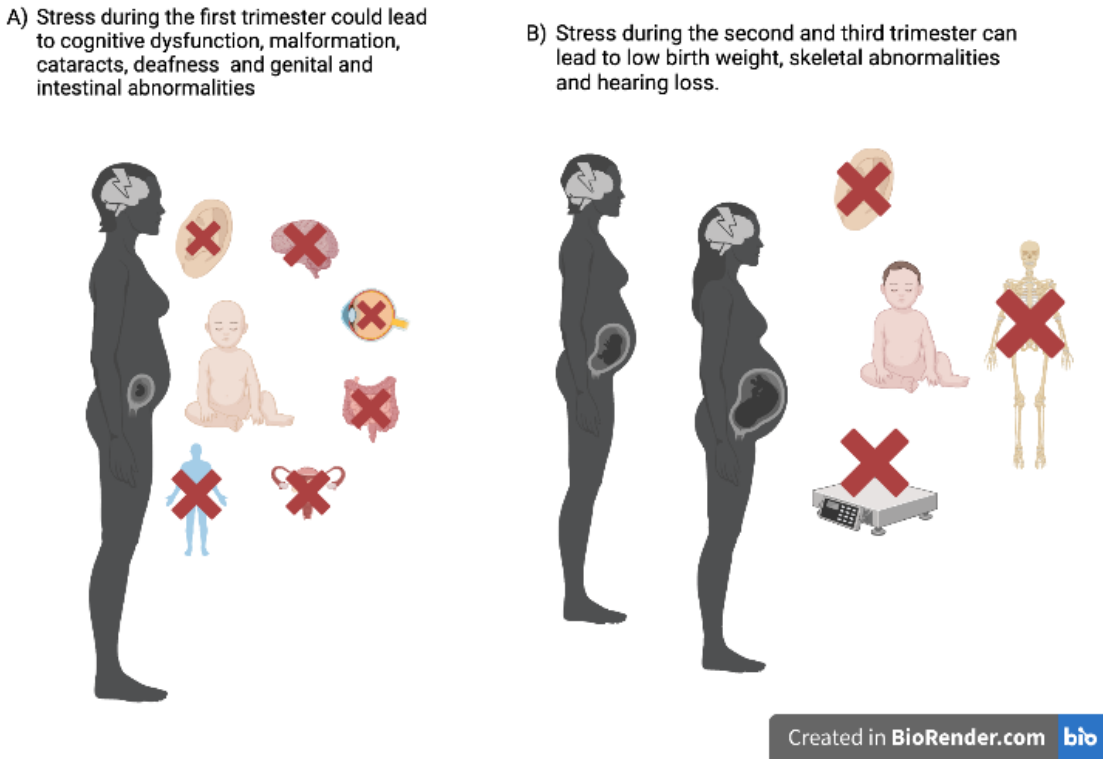

Figure 2. The image depicts what can happen to the human body if the individual experiences stress while pregnant. (A) Exhibits susceptible organs that are prone to developmental impairment to the fetus if a pregnant individual repeated extreme stressful stimuli during their first trimester. (B) Shows the possible consequences of experiencing repeated stress during the 2nd and 3rd trimesters of pregnancy. All panels in the figure were created with BioRender

Acute and Chronic Exposure to Stress in Adulthood

Stress during adulthood can impact most of the body's organisms. While it can impair memory due to increased hippocampus function 36, 1, others have reported enhanced memories regarding events experienced during high-stress levels 1, 34. It causes changes in the dendrites (debranching and shortening), which take ten days to change to their usual size. It also impairs spatial learning and is reversed 21 days later 52, 1.

In addition to neuronal changes that occur after a stressor, an individual's body is also affected. Mainly, when stress becomes chronic, our diets cannot quickly replace the calcium depletion, so our bones are constantly being leached of calcium, (Figure 3) leading to potentially more porous bones, brittle bones, and osteoporosis 3. There is a strong association of obesity with chronic low-grade inflammation in premenopausal women 54. This pro-inflammatory state and altered neuroendocrine and cardiovascular stress responsiveness may conceivably constitute one of the mechanisms linking psychological stress and the long-term health risks associated with obesity 53. (Figure 3)

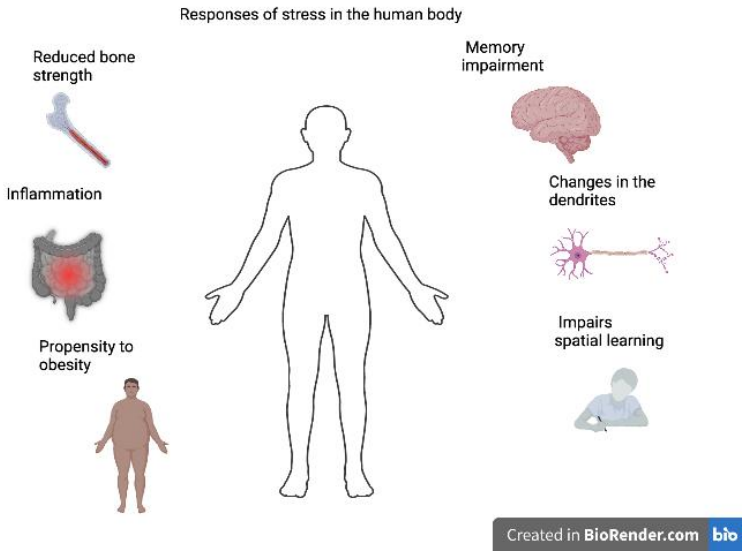

Figure 3. The image above shows bodily responses to stress in an adult human. They include: reduced bone strength, memory impairment, changes in the dendrites, impairment of spatial learning, inflammation in the stomach, and a propensity to obesity. All panels in the figure were created with BioRender

The research study investigating the effects of stress on physiological variables in obese women compared to non-obese women found that obese women exhibited a more robust cortisol stress response and higher heart rate and diastolic blood pressure following stress than their non-obese counterparts. Additionally, obese women had higher levels of the inflammatory marker IL-6 before and after stress and higher baseline levels of circulating leukocytes, granulocytes, CD3+ cells, and hs-CRP 15. However, the study also noted that stress led to a significant increase in IL-6 concentrations in non-obese women, thus suggesting a possible link that stress can induce changes in pro-inflammatory pathways regardless of body composition. 14,15.

III Discussion

This review article explores the effects of stress during vaious stages of development and its impact on cognition. Stress can be categorized as chronic, which is a prolonged exposure to adverse circumstances, or acute, which is a response to specific stressful situations. The activation of the hypothalamus-pituitary-adrenal (HPA) axis and the release of glucocorticoids play a significant role in the stress response 59.

In young children and during early adolescence, research has shown that stress can lead to a decrease in the size of the hippocampus,60 which can have detrimental effects on brain development when compared to individuals who are not exposed to similar stress 10. Additionally, stress has been observed to have negative impacts on cognitive performance, including academic achievements and tasks that go beyond traditional educational assessments36. In adults, chronic stress impairs memory due to increased hippocampal function 36,1. Furthermore, changes in dendrites size and arborization enhances fearful memory, which take time to regulate 36,34. Chronic stress can impair spatial learning, but these effects can be reversed after a certain period1. The effects of chronic stress in adulthood are generally reversible, while for infants, they tend to be permanent 57 56, 1.

The review also highlights the impact of stress during pregnancy, which can affect the dopaminergic system of the baby, making them more susceptible to addictive behaviors 1,58. Stress exposure during pregnancy can lead to lower weight and size in the baby and have long-lasting effects on the child's physical development 2, 65 .

Furthermore, stress in adulthood can have various impacts on the body, including impaired memory,52 changes in dendrites,1 and negative effects on bone health,3 cardiovascular function, and obesity-related inflammation 14. Overall, this review emphasizes the detrimental effects of stress on different stages of development and cognition. Understanding these effects can help raise awareness and inform strategies for managing and reducing stress-related risks.

Other questions or topics you may want to further investigate may be: How does chronic stress affect the volume of the hippocampus in young children and early adolescence? What are the long-term consequences of stress exposure during pregnancy on the development of the child? Can the negative effects of stress on cognition in young children and adolescents be reversed? How does chronic stress impair memory in adults? What are the mechanisms behind the enhancement of fearful memory under stress? How do changes in dendrites occur in response to stress, and how long does it take for them to regulate? Are the effects of chronic stress reversible in all aspects of adulthood, or are there specific areas where the effects persist? What are the specific cognitive deficits associated with stress exposure in young children and adolescents? How does stress contribute to obesity-related inflammation, and what are the long-term health risks associated with this? Are there effective strategies for managing and reducing the negative effects of stress on development and cognition? Although many studies have lead to a better understanding regarding the demential affects of stress during various stages of development, a greater focus is now necessary to better understand how persistent physiological responses can be medigated in not only adults but all developing children. Within this review, we hope to have elicidated the current knowledge regarding acute and chronic stress and within the scope of in utero through adulthood.

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