

The Impact of Chemical Changes in The Brain Caused by Chronic Stress Can Trigger Depression

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ABSTRACT

The present research has attempted to study the link between chronic stress, the chemical changes in the brain caused by it, and depression. Chronic stress (also known as chronic strain) has been defined in a variety of ways, but it usually refers to one or more types of stress that have persisted for at least many months. Numerous chemical changes occur in the human brain when the human body is subjected to chronic stress over a lengthy period. Chronic or ongoing stress can cause several psychological and physiological problems and stress has been found to influence brain chemicals including cortisol and corticotropin-releasing factor. Cortisol levels that are elevated for an extended period have been related to mood disorders and hippocampus shrinkage in the brain. Stress is a key contributor to chronic inflammation in the body. Furthermore, diabetes and heart disease can also be caused by chronic inflammation. Chronic stress elevates cortisol levels in the blood and has an effect on serotonin levels in the body. This contributes to the fact that continuous stress causes a series of chemical changes in the human brain, which may simply make the individual more prone to developing depression or relapsing (the condition is prone to recur in someone who has recovered). These physiological and biochemical changes make the human body more sensitive to depression and make it more likely to acquire the mental illness (known as Major Depressive Disorder). The current study examined many research studies that support a substantial relationship between chronic stress and depression.

Keywords: *Chronic stress, Brain, Chemical changes, Depression*

We all experience stress to varying degrees and as a result of various causes and conditions that occur to us or in our environment. Stress is a common experience for humans because we all respond or react differently to different situations, challenges, and changes in our lives. Stress, according to Hans Selye (1950), is "the non-specific response of the body to any demand." Until Selye (1936) suggested using the expression "stress" to describe how it was when an organism was subjected to an unpleasant stimulus the phrase was not linked to human behavior. The physical consequences of stress were separated from other physical symptoms experienced by patients via his study in 1950 by Selye. He found that individuals were not directly affected by their sickness or medical condition.

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Stress may also be characterized as the response to threats or challenges of physical, emotional, cognitive, and behavioral components. Some people are more sensitive to the impacts of stress than others, since what one person perceives as a threat, another perceives as an opportunity. Stressors are occurrences that cause stress, in a simpler way, events that cause stress. Stressors might originate from within a person or from outside sources, and they can range in severity from mild to severe. In terms of range, the stressor can be merely irritating like constant loud music from the neighbor's house, or deadly serious like a hurricane approaching your city. Stressors can even also be imaginary. Imaginary stressors are those that are not real, such as societal pressure, guilt, and jolts to self-esteem, such as failure or fear of failure, indecision, and so on, among others (Kolhatkar, 2013).

Two types of stressors exist those that create distress and those that cause eustress. Distress is caused by unpleasant stressors, whereas eustress is caused by good occurrences that nonetheless need the individual to adapt or adjust. When good circumstances force the body to adapt, Hans Seyle (1936) first used the term eustress. Hans Seyle (1936) introduced the word eustress to describe the stress that occurs when good circumstances force the body to adapt. Researchers have updated Seyle's original concept to describe eustress as the ideal amount of stress that humans require to promote health and well-being. Because distress is generated by a negative event in one's life, it is also known as a negative life event stressor, whereas eustress is created by a positive event and is known as a positive event stressor. Furthermore, unpleasant feelings, bodily illnesses, diseases, and maladaptive behavior are all indications of distress. As a result, stress is frequently associated with distress.

Zautra and Reich (1983) discovered the same domain effect when comparing positive and negative experiences in life. Negative events cause distress and lower one's quality of life. Positive events, on the other hand, boost positive sentiments and improve one's quality of life. However, the same domain effect obscures the reality that people's negative reactions are stronger than their positive reactions. In other words, individuals respond more intensely to negative occurrences than they do to positive events (Baumeister et al., 2001). Good and negative events can differ in a variety of ways other than their valence. Even when positive and negative events are equal, negative events cause more distress than positive events produce eustress.

However, based on available data, a research study (Bienertova-Vasku, Lenart, & Scheringer, 2020) argues that there is no such thing as eustress. The adaptation reaction is neither positive nor negative, and its influence on longevity or performance is decided by several other interactions between the body and its surroundings (not only with the stressor itself). Furthermore, various studies promote that, the difference is not just in the level of stress, but also in how the individual understands the event. The same stressor can cause distress in one person and eustress in another, but a more positive view of a stressor leads to more positive coping with it (Fevre et al., 2006; Sarada & Ramkumar, 2014).

Stressors can be environmental as well as psychological. Environmental stressors are external stresses that can be classified as catastrophes, major life changes, or hassles. Psychological stressors are pressure (the psychological feeling brought on by externally imposed urgent demands or expectations for a person's behavior), uncontrollability (the degree of control that a person has over a certain event or situation), frustration (the psychological state brought on by the failure to achieve intended goals or the satisfaction of a perceived need), conflict (or whenever two or more conflicting and incompatible interests, ambitions, or behaviors are at odds with each other). Other than that, there are physiological

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stressors too. Hunger or food deprivation, sleep deprivation or sleeplessness, severe hyper- or hypothermia, and drug withdrawal states are typical physiological stressors. Numerous psychoactive medications also serve as pharmacological stressors due to their constant and excessive usage (Sinha, 2008).

There are two types of stress, acute stress and chronic stress, each of which has varying effects on the mind and body. Events or situations that are unexpected, unpredictable, pose a threat to the ego, or create a loss of control can lead to acute stress. This sort of 'on-the-spot' stress might be beneficial when the stress hormones are released to help your mind and body in dealing with the circumstance. Chronic stress, on the other hand, this stress caused by frequent exposure to conditions that cause stress hormones to be released. This sort of stress may wear out your mind and body. Many researchers estimate that our stress response system was not intended to be triggered continuously. This excessive usage may contribute to the collapse of several physiological systems. The more prolonged, repeated, or chronic the stress—for example, states associated with increased distress intensity or persistence—the greater the unpredictability and uncontrollability of the stressful situation, the lower the sense of mastery or adaptability, the greater the magnitude of the stress response, and the risk of persistent homeostatic dysregulation. Thus, understanding the function of stress in raising the likelihood of maladaptive behaviors requires consideration of the characteristics of intensity, controllability, predictability, mastery, and adaptability (Sinha, 2008).

Chronic Stress

Our bodies are well-equipped to deal with stress in short doses, but when that stress becomes long-term or chronic, it can have significant consequences for the human body. Chronic stress (or chronic strain or difficulty) has been described in many ways, but it typically refers to one or more kinds of stress that have been present for at least several months (e.g., poverty, marital distress, medical problems, having a child with a disability). The American Psychological Association has defined chronic stress as, “the physiological or psychological response to a prolonged internal or external stressful event (i.e., a stressor). The stressor need not remain physically present to have its effects; recollections of it can substitute for its presence and sustain chronic stress.” Chronic stress is prolonged that’s why it is also called long-term stress.

Over time, the definition of chronic stress has changed greatly. Different researchers have utilized their findings to back up various definitions of chronic stress. For example, Brown and Harris (1978) discovered that instances of depression were much more likely to have had either an ongoing problem or at least one major life event before onset, defining chronic stress as "ongoing difficulties lasting at least 4 weeks." Brown's research has not distinguished or contrasted the effects of chronic and acute stress, but Rojo-Moreno et al. (2002) used the same methodologies as Brown and colleagues to find an equivalent prediction of depression from acute stressors and ongoing issues. Breslau and Davis (1986) defined chronic stress in women as having a child with a disability and discovered that such experiences were associated with more lifetime occurrences of severe depression but not with higher rates of present depression in such women when compared to nonstressed controls. Chronic stress is also defined as a lack of social support, has also been linked to depression (e.g., Paykel & Cooper 1992). We measure chronic stress, as usual, ongoing circumstances for at least 6 months across many dimensions of adult role functioning, following Mazure's guidelines (1998).

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Various research studies also question the relationship between chronic stress and acute stress. Brown and Harris's study has shown that an acute incident that "matches" a continuing issue increases the risk of depression (1989). A few additional studies have looked at both types of stressors and concluded that the effects of acute stress–depression connections may be changed by chronic stress or that the effects of the two forms of stress may differ and further according to another research study (Hammen, Kim, Eberhart, & Brennan, 2009), which investigated whether chronic stress has an independent or interactive relationship with acute life events in their association with the onset of major depression, the findings confirmed the importance of chronic stress in three ways. First, chronic stress, along with acute life events, was independently linked with the onset of Major Depressive Episode (MDE) but the latter showed a greater relationship with depression, comparable to prior findings reported by Brown and Harris. Second, higher levels of chronic stress were related with higher levels of acute stress, which comprised both total life events and stress generation—events that were dependent upon the individual. Third, there was a trend for chronic stress to moderate the effects of acute events on major depression, such that high levels of chronic stress amplified the impact of acute events, whereas the association between acute stress and depression was lower among women with lower levels of chronic stress.

The Impact of Stress on The Brain

When exposed to a perceived stressor, the body experiences a series of biological changes. This is the result of two different processes in act. The sympathetic-adrenomedullary (SAM) system is intended to organize resources and prepare for a fight-or-flight response (Gunnar & Quevedo, 2007). The stress response originates in the hypothalamus, which activates the sympathetic nervous system (SNS). This, in turn, stimulates the adrenal medulla (the inner section of the adrenal glands) to release adrenaline (also known as epinephrine) and noradrenaline (norepinephrine). These induce a rise in heart rate and cause the body to absorb glucose more quickly as they circulate through the blood. The hypothalamus-pituitary-adrenal (HPA) system is the second system implicated in the stress response. The hypothalamus, in addition to activating the SNS, secretes a hormone known as corticotropin-releasing hormone (CRH). This hormone stimulates the pituitary gland as it travels through the bloodstream. Adrenocorticotrophic hormone is then secreted by the pituitary gland (ACTH). This causes the adrenal cortex (the outer section of the adrenal gland) to generate glucocorticoids, which are stress hormones.

Stress glucocorticoid cortisol is generated in humans. This hormone is useful to have on hand in case of emergency. As a result, the body is more prepared to fight or run. Additionally, it suppresses the innate immune system's reaction to infection. The body's inflammatory reaction to an injury will be delayed as a result of this. To put it another way, escape takes priority over mending, and tissue regeneration comes second to remaining alive. Yet, cortisol also has a drawback. It has been shown that cortisol can harm brain cells, especially in the hippocampus, if the reaction is not cut off (Sapolsky, 2000). Stress is terrible for your brain on a fundamental level. In some cases, it might even slow down the rate of growth. Following this, the brain has receptors for cortisol detection. After being engaged, they transmit a feedback message meant to decrease the action of stress-related hormones. Stress-induced activation of the HPA axis and cortisol release continues as long as the stressor persists. However, a persistently hyperactive HPA axis with high cortisol levels in the bloodstream may be harmful.

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Interestingly, a study (Kolhatkar, 2013) shows how the left and right brains operate differently under stress. According to Jil Taylor, the left brain is capable of analysis, reasoning, mathematics, and so on. It is where the language function is located. It is in charge of memorizing facts in timely sequences. It continually feeds us concepts based on language and informs us who we are. It preserves the feeling of hierarchy and is connected with ego, ambition, and so forth. Fear, worry, and stress are more prevalent as a result of left-brain activation. It also fosters ideals and discipline while suppressing natural inclinations and emotions (Superego). The right brain, on the other hand, is naturally creative. It views all beings to be equal and takes a holistic approach to everything. It recognizes body language, tone of speech, and so on. This portion of the brain's feelings is calm and joyful. In general, this portion of the brain is fearless. It most likely has just a minimal function in stress generation. Balanced activity in both brains results in balanced behavior. In today's world, there is a general prevalence of the left brain, which our culture encourages from childhood onwards. This sort of left-brain predominance is the source of increased "stress" experiences.

Depression

One in every five persons will have a good condition over their lives (Kessler et al, 2005; Kessler et al, 1993). Major depressive disorder (MDD), the most common mood disorder (6.7%) (Kessler et al, 2005), is the main cause of disability globally (Lopez and Murray, 1998). Depression, which often comprises emotions of extreme sorrow and dejection, is one of the major moods associated with mood disorders. Some individuals with mood disorders only have sad moods for short periods or episodes. The most frequent type of mood disruption is a depressive episode, in which a person is significantly sad or loses interest in formerly enjoyable activities (or both) for at least two weeks, as well as additional symptoms such as changes in sleep or food, or feelings of worthlessness (According to the DSM-5 for diagnostic criteria).

A major depressive disorder (major depressive disorder) is a frequent and significant medical condition that adversely affects one's mood, thinking, and behavior. The fact of the matter is that it's also treatable. People who suffer from depression report feeling sad or losing interest in things that they previously cherished. Your ability to perform at work and home might be affected and cause serious impairment in major areas. Symptoms of depression can range from mild to severe, and include: sadness or a depressed mood, changes in appetite — weight loss or gain unrelated to dieting, trouble sleeping or sleeping too much, fatigue or a lack of energy, and an increase in purposeless physical activity (e.g., pacing, hand-wringing, inability to sit still). Other symptoms include slow motions or speech, a sense of worthlessness or shame, trouble thinking, focusing or making decisions, and thoughts of suicide or death.

For depression to be diagnosed, you must have symptoms that persist for at least two weeks and show a change in your level of functioning from before. Anyone can be affected by depression, even if they appear to be living in a pretty good environment. In addition to biochemistry, variations in specific brain chemicals may contribute to depression's symptoms, and genetics and heredity point out that depression can run in families. It is estimated that 70 percent of a pair of identical twins are more likely to suffer from depression at some point in their life (Torres, 2020). In addition, persons with poor self-esteem, who are easily overwhelmed by stress, or who have a pessimistic outlook on life tend to be at greater risk of developing depression. Environmental risk factors also highlight

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that chronic exposure to violence, neglect, abuse, or poverty may make certain people more prone to depression.

Responses to a severe loss (e.g., bereavement, financial ruin, natural catastrophe losses, a catastrophic medical disease or disability) may involve emotions of great grief, rumination over the loss, sleeplessness, poor appetite, and weight loss, which may mirror a depressive episode. Although such symptoms may be understood or thought to be acceptable in light of the loss, the occurrence of a severe depressive episode in addition to the typical response to a large loss should be carefully evaluated. This option invariably necessitates the use of clinical judgment based on the individual's history and cultural norms for expressing pain in the context of bereavement.

Relationship Between Chronic Stress, Brain, And Depression

Because stress may have a major impact on our brains, we are more susceptible to physical and psychological problems. Chronic or persistent stress can lead to a variety of psychological and physiological imbalances.

Prolonged stress has been shown to affect brain chemicals such as cortisol and corticotropin-releasing factor. Cortisol levels that are too high for too long have been linked to mood disorders and hippocampal atrophy in the brain. The decreased hippocampus caused by chronic exposure to stress hormones and inflammation is more frequent in depressed individuals than in healthy persons (Clark, Chamberlain, & Sahakian, 2009). According to a research study (Gianaros et al., 2007), chronic stress reduces the volume of the hippocampus, a brain region that supports learning and memory and regulates neuroendocrine activity in nonhuman animals. Surrogate and retroactive markers of chronic stress are also associated with reduced hippocampus volume in people with stress-related psychiatric disorders defined by poor learning and memory and dysregulated neuroendocrine activity. Repeated stress is a major cause of chronic inflammation in the body. Chronic inflammation can cause a variety of health issues, including diabetes and heart disease (Dregan, Charlton, Chowienzyk, & Gulliford, 2014).

Acute and severe stresses that are unavoidable in adulthood can have long-term effects on the brain and behavior. Most 'chronic stress' models involve subjecting an organism to many weeks of daily immobility, a selection of randomized stressors twice daily, or repeated social stressors. A blood-brain barrier typically protects the brain from circulating molecules. However, when subjected to repeated stress, this barrier becomes permeable, allowing circulating inflammatory proteins to enter the brain (Ménard, Pfau, Hodes, & Russo, 2017).

In human studies, inflammation has been found to have a negative impact on brain systems associated with motivation and mental agility. According to a research study (Felger et al., 2016), in depressed individuals, inflammatory biomarkers (such as cytokines and C-reactive protein (CRP)) are consistently increased and inflammation is one pathophysiological mechanism that might be driving these alterations. Furthermore, inflammatory stimuli diminish neuronal activity and dopamine release in reward-related brain areas, which is associated with decreased motivation and anhedonia.

Clinical investigations have found that circulating oxytocin correlates adversely with depression symptoms (Scantamburlo et al, 2007) and is lower in MDD patients. Clinical research (Frasch et al, 1995) found that depressive individuals had lower nocturnal oxytocin

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(OT) production than age-matched controls. Despite the anticipation surrounding oxytocin treatments, much more research is required to completely understand oxytocin's involvement in immunological function and depression.

Serotonin is one of the chemicals in the brain that are affected by chronic stress. As well as being important for mood regulation, serotonin is also important for well-being. Depressed patients take selective serotonin reuptake inhibitors (anti-depressants) to restore serotonin's functional activity in the brain.

Limitations And Gaps

The link between chronic stress, the brain, and depression has been studied on a variety of platforms. The limitation of the study would be a lack of experimental investigation, which would confirm terms of physiological and biological properties. In addition, there is a lack of cultural background. None of the research studies reviewed in this particular secondary research compare the difference in intensity between acute and chronic stress.

CONCLUSION

Depression can be caused by several reasons, such as genetics, brain chemistry, and also one's present living situation. Chronically stressful life situations may increase your risk of developing depression if you do not manage the stress properly. Chronic stress is well recognized to produce depression, which is a major cause of disability worldwide. It is also a recurrent illness; those who have previously had depression are more likely to experience it again, especially when under stress. Several research papers in this review indicate that prolonged stress can cause numerous chemical changes in the brain, which can contribute to the development of the disease. Chronic stress raises the level of cortisol in the circulation and affects serotonin levels in the body. Furthermore, depression can have far-reaching repercussions. Recent research has shown that depression affects cognition in both non-emotional domains, such as planning and problem-solving, as well as emotional and social domains, such as producing an attentional bias to negative information. The present study has analysed and evaluated different research studies that demonstrate that during prolonged stressful situations, the human brain undergoes a sequence of chemical changes that may just make the person more prone to develop depression or relapse (someone who has recovered from the disorder is likely to develop it again).

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Conflict of Interest

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