THE BIOLOGICAL AND NEUROLOGICAL CHANGES IN THE ADULT BRAIN DUE TO CHRONIC ANXIETY, STRESS, AND DEPRESSION

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ABSTRACT

Health conditions including long-term anxiety, stress, and depression have become

increasingly prevalent in today's society. These conditions have been said to have reached epidemic levels while they also significantly impact a vast percentage of the adult population. Also referred to as mental health disorders, these conditions are often exacerbated by factors such as modern lifestyle demands and environmental stressors. Consequently, not only do they impact patients' emotional well-being but they also induce substantial biological and neurological changes in the adult brain. In essence, prolonged exposure to stress is noted to activate the hypothalamic-pituitary-adrenal (HPA) axis, resulting in cortisol dysregulation. Thus, affecting critical brain regions such as the hippocampus, amygdala, and prefrontal cortex. As a result, these regions undergo structural modifications, including hippocampal atrophy, prefrontal cortex thinning, and amygdala hyperactivity. Ultimately, this contributes to cognitive deficits, emotional dysregulation as well as persistent symptoms of depression and anxiety. Recent studies have highlighted the roles of neuroinflammation, oxidative stress, and neurotransmitter imbalances in the pathophysiology of these disorders. According to studies, elevated levels of pro-inflammatory cytokines and reactive oxygen species interfere with neuroplasticity and synaptic functioning, while disruptions in serotonin, dopamine, and

norepinephrine systems further impair mood regulation. Additionally, epigenetic modifications and reduced expression of brain-derived neurotrophic factor (BDNF) have also been associated with long-term stress exposure, a revelation of a deeper molecular basis for the chronicity of these conditions. It is noteworthy that despite these adverse effects, the adult brain has the capacity to

3 retain a degree of plasticity that goes on to enable recovery through targeted interventions. These interventions include pharmacological treatments, psychotherapy, and lifestyle modifications. Additionally, some emerging therapies like transcranial magnetic stimulation (TMS) hold great promise for reversing and mitigating brain damage.

Introduction

In the past, conditions including chronic anxiety, stress, and depression were increasingly recognized as psychological issues. However, in recent times, these conditions have been noted to have profound neurological and biological consequences for those affected. Consequently, these mental health disorders are becoming highly prevalent in the global world. This epidemic is highly influenced by factors including socio-economic stressors, environmental challenges, as well as lifestyle changes. According to the World Health Organization (2023) study, depression affects millions of people globally, while anxiety disorders have been said to be among the most common mental health

conditions. It is worth noting that the adult brain, especially during one's midlife and older stages of life, is vulnerable to the cumulative effects of these disorders. It is important to have a better understanding of the biological and neurological underpinnings of anxiety, stress, and depression for the effective development of workable interventions. Recent studies have shown how chronic psychological distress affects brain structure and function, in particular, within regions associated with emotional regulation, memory, and executive functioning. That said, this paper will explore the biological mechanisms and neurological alterations associated with chronic stress, anxiety, and depression in adults, as informed by recent peer-reviewed studies.

The Stress Response and the HPA Axis Usually, under stress, the hypothalamic-pituitary-adrenal (HPA) axis is activated. This system goes on to regulate the release of cortisol, which works by helping the body manage short-term threats. However, if one has persistent stressors, chronic activation of the HPA axis is due to occur, leading to dysregulation of cortisol levels, a state that can result in neurotoxicity 5

over time (Kline & Mega, 2020).

Studies have gone on to demonstrate that when one is exposed to prolonged elevated cortisol levels, this may lead to hippocampal atrophy, particularly in the CA3 region; a crucial region for learning and memory (Won & Kim, 2020). Furthermore, dysfunction of the HPA axis is said to contribute to the persistence of depressive and anxiety symptoms while it is also linked to reduced neurogenesis in the adult brain. Structural and Functional Brain Changes Several brain regions including the hippocampus, prefrontal cortex, and amygdala are significantly affected by chronic anxiety, stress, and depression. These areas play vital roles in cognitive and emotional processing. Firstly, the hippocampus is notably sensitive to stress hormones. In an adult patient with chronic depression, hippocampal volume is notably reduced. Studies have noted that chronic stress reduces neurogenesis and dendritic branching in the hippocampus (Leschick et al., 2021). In turn, this leads to impairments in memory and emotional regulation. Consequently, this structural degeneration causes cognitive deficits commonly seen in depressive disorders.

The prefrontal cortex (PFC) is another region that is highly impacted by the aforementioned stressors. The region is essential for decision-making, attention, and regulationof emotions. Usually, chronic stress impairs synaptic connectivity in the PFC and reduces dendritic arborization, leading to loss of executive function as well as increased vulnerability to emotional dysregulation (Woo et al., 2021). Thirdly, the amygdala, a region that processes fear and threat is noted to exhibit increased activity in people with anxiety and depression. Unlike the

aforementioned two regions, the amygdala often shows hypertrophy and increased dendritic growth under chronic stress. In turn, it may exacerbate hypervigilance and negative emotional 6 responses sustaining the disorders.

Neuroinflammation and Oxidative Stress

Studies have shown neuroinflammation to be a key contributor to the pathophysiology of depression and anxiety (Smith & Pollak, 2020). In essence, chronic stress is noted to promote the release of pro-inflammatory cytokines including IL-6, TNF-α, and CRP, which go on to disrupt normal neuronal function and plasticity (Xu et al., 2020). The manifestation of these inflammatory markers correlates with symptom severity and reduced response to traditional antidepressants (Maes et al., 2024). Oxidative stress also plays a significant role, as reactive oxygen species (ROS) damage neuronal membranes and mitochondria. Chronic psychological distress impairs the antioxidant defense system, leading to neuronal dysfunction and apoptosis.

Neurotransmitter Dysregulation

The aforementioned mental health disorders are also seen to be closely linked to imbalances in neurotransmitters, particularly serotonin, dopamine, and norepinephrine. As one may know, these chemical messengers work by regulating one's mood and cognitive performance. Reduced serotonin

activity is a result of a depressive disorder and has been linked to increased amygdala reactivity and impaired connectivity in mood-regulating circuits (Samaripour, 2025). With dopamine depletion, especially in the mesolimbic pathway, one may manifest with anhedonia and a lack of motivation. Additionally, decreased norepinephrine hinders one's ability to pay attention and be alert, compounding the cognitive deficits seen in

chronic anxiety and depression.

Epigenetic and Cellular-Level Changes

7 Epigenetic modifications, including DNA methylation and histone acetylation, have been increasingly recognized as mediators of the long-term effects of stress. Usually, stress-induced epigenetic changes go on to silence genes involved in neuroplasticity and neurogenesis. In turn, this leads to persistent alterations in brain function. Long-term stress could also affect brainderived neurotrophic factor (BDNF), which is a protein vital for neuron survival and plasticity. Studies have shown reduced BDNF expression, particularly in the hippocampus, in individuals with depression and anxiety, which correlates with symptom severity and treatment resistance (Arosio et al., 2021).

Intervention and Neuroplasticity

This study found chronic anxiety and depression to cause extensive damage to the human brain. Nevertheless, an intervention for the recovery of the adult brain is possible through neuroplasticity. Studies have pinpointed recent interventions ranging from pharmacological approaches to the use of antidepressants like ketamine therapy (Rădulescu et al., 2021).

Similarly, psychotherapeutic approaches like cognitive-behavioral therapy (CBT) have also been suggested in promoting the restoration of neural function. Other interventions can include exercise, mindfulness meditation, and incorporating adequate sleep. These have been shown to reduce stress, lower inflammatory markers, and enhance neurogenesis (Tian et al., 2025). For instance, physical exercise has been linked to improved memory function, executive function, as well as reward processing in depressed individuals (Tian et al., 2025). Other emerging treatments such as transcranial magnetic stimulation (TMS); a non-invasive technique, work by targeting dysfunctional brain circuits and rapidly enabling synaptic plasticity (Jannati et al., 2021). In turn, such an approach holds great promise of improving health outcomes in patients with mental health disorders

Conclusion

8 Mental health disorders including chronic anxiety, stress, and depression do not only affect the emotional well-being of individuals but are seen to also impact both biological and neurological well-being. From HPA axis dysregulation and neurotransmitter imbalances to neuroinflammation and cellular damage, the aforementioned disorders affect numerous layers of neural functioning. It is noteworthy that if left untreated, they can pose negative health outcomes including cognitive decline, low quality of life, and a heightened risk of developing neurodegenerative diseases. Nevertheless, this study found the adult brain to have remarkable

plasticity, which offers hope for restoration. It is important that patients seek timely and appropriate interventions such as pharmacological, psychological, and lifestyle-based approaches to restore brain function. More research is also necessary to gain further understanding of the biological mechanisms of mental illness. This way, it may lead to the development of more effective treatments that can help address the global mental health epidemic.

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