Review

Neuronal circuits of stress and their dynamic interactions: a biopsychological framework

L.A. Cacha* and R.R. Poznanski
Integrative Neuroscience Group, http://www.intneuroscience.org

*Correspondence: lcacha@intneuroscience.org (Lleuvelyn A. Cacha)
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Abstract

Stress alters neuroendocrine, autonomic, and behavioral processes to cope well with perceived threats that compromise subjective wellbeing. Just as the perception of risk can change the structure and function of brain circuitry, which may result in enduring behavioral changes. There needs to be a greater understanding of how the brain reacts to stress-related disorders and discern how the adaptation mechanisms of the central nervous system under acute stress, as well as how stress-induced adaptation mechanisms are altered under chronic stress conditions that may induce plasticity-related changes in the brain. During this interaction, the brain becomes more capable of resolving stress in a way that is either adaptive or maladaptive, leaving the most critical deficit in the emotion regulation associated with risk for pathological conditions. The essence of this associated risk involves the reciprocal influence between hypothalamic-pituitary-adrenal function, the relay nucleus within the amygdala reactivation, and the hippocampus as essential structures associated with the forebrain pathways mediating stress-induced hormones, and the gamma-aminobutyric acid neurotransmitter system as key mechanisms of regulating stress. Understanding how related emotional experiences occur on the neural level and their impact on cognition and behavior entail tracing the interaction between the hypothalamic-pituitary-adrenal axis, the hormones released by these structures, and the neuroendocrine system's reactivity to stress. The interaction between threat-sensitive brain circuitry and the neuroendocrine stress system is crucial to understanding how related emotions arise on the neural level and their impact on cognition and behavior. The hypothalamic-pituitary-adrenal axis is critical in regulating the synthesis and release of endocrine hormones through its interactions with these structures, collectively referred to *as* the *stress response.* The stress system is described in its anatomy and physiology and connections to other brain areas and endocrine systems. We explore the current evidence linking stress with pathophysiologic mechanisms implicated in stressful conditions affecting the neuronal circuitry between endocrine, metabolic, gastrointestinal, and immune systems. Examining the biopsychological contributions provides a conceptual framework for understanding the emergence of emotions and stress-related behaviors.

Keywords: Stress response, amygdala, anxiety disorder, emotion control and regulation, GABA neurotransmitters, homeostasis, HPA axis, neural circuitry, stress hormones, affective neuroscience, glucocorticoids

1. Introduction

The interplay between cognitive and emotional processes has long been recognized as a dynamic, multi-level brain interaction that simultaneously impacts behavior and physiologic responses. During stress, emotions are likely to respond to the multicomponent of cognitive processes that arise as adaptive responses in anticipation of stimuli that threaten homeostasis. Thus, the body modulates various physiologic and behavioral processes to maintain optimal balance. Physiological systems are constantly fine-tuned to preserve predefined steady states (homeostasis and eustasis) underlying adaptation to foster physiological responses underlying successful adaptation and resilience in maintaining the body's health and well-being [1, 2]. These systems-level physiological changes ultimately reflect a highly interconnected neuroendocrine, cellular, and molecular network required for adaptive stress response. An imbalanced stress response system connected with chronic stress can severely disrupt the body's self-regulation and ultimately lead to pathologic states (allostasis) with a spectrum of clinical manifestations [2, 3].

Converging evidence provide that repeated exposure to stress negatively impacts health, behavior and sense of well-being. Under prolonged physical or psychological stress, these mechanisms become dysregulated, and the connectivity between brain regions becomes unbalanced, resulting in pathological behaviors [3]. Although stress responses are essential for a basic survival mechanism, individuals differ in their perception and adaptation under conditions involving threat, conflict and pressures. Stress involves the alteration of physiological systems that constitute a threat to homeostasis that, when experienced over time, can lead to chronic stress, which is a factor that influences illness expression [3, 4]. This could both result from and contribute to over activation of neuronal circuits that control stress responsiveness, anxiety, and emotion. The neural dynamics of emotions

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may evolve in response to different affective states that may be conceptualized and consciously related to the multicomponent cognitive processes that generate them as adaptive responses in anticipation of stimuli that threaten homeostasis [4-6].

The brain mechanism of affect underlying perception and cognitive appraisal of a situation is likely to activate specific brain circuits that instigate affective experience related to the behavioral responses associated with stress and anxiety [6-8]. Ultimately, these mental representations of the interpreted context and the subjective quality of affective states play a significant role in developing future behavioral and emotional tendencies [9,10]. This behavioral experience accompanies spontaneous physiological and emotional reactions. Previous research findings [11,12] identified these reactions associated with emotions ultimately facilitate adaptive responses to environmental challenges and boost memory presentation, to a certain extent enabling the famous "fight or flight" reaction. The human brain and its context-dependent response functions, including cross-level integration of signaling structures and circulating hormones, are sophisticated and flexible.

The study of Raz and associates [13] examines emotions emerging from the neurodynamics of many interacting brain systems, like how neurons behave concerning emotions can substantially influence cognitive processes and impact different systems that have specialized functions in doing the body works [14]. In this intriguing reciprocal connection, underlying emotional processing in the brain transmits to bodily changes associated with emotion-specific expression, cognition, and motivated behavior to even assimilate the conscious experience of being stressed.

Understanding how the brain reacts to stress-related disorders and discovering how the central nervous system can adapt under acute conditions and how these mechanisms change under chronic stress are necessary. An analysis of how chronic stress affects the mind and body and how the mind coordinates the body to maintain internal equilibrium and achieve optimal function. It is essential to fully understand the physiological regulatory mechanisms inside the brain to maintain stable psychological well-being and react quickly to stressful situations.

2. Neural communication via the nervous and neuroendocrine system

There are intricate and reciprocal connections between the neural circuits regulating emotional behaviour. Several brain areas interact structurally, enabling flexible, coordinated functioning, such as in the limbic system [15, 16]. An integral part of the emotional brain is the system, where interacting subcortical structures intersect with the cerebral cortex [17, 18]. The amygdala, located near the hippocampus, interconnecting with other limbic system components, is responsible for many aspects of emotions, including recognition of facial expressions of fear and anxiety-related memories [19-21]. Alternatively, the amygdala may register emotional stimuli and initiate coordinated physiological and behavioral responses that underlie defensive reactions [22, 23].

Some studies have shown, using functional magnetic resonance imaging (fMRI), that these brain regions where the amygdala as being directly responsible for immediate reaction associated with conditioned fear, become active when experiencing anxiety [24-27] which generally helped to shed light on the underlying neurobiological causes of fear, stress and anxiety [28, 29]. The amygdala attends to various functions throughout the limbic system and plays an important role in regulating emotions and memories. In addition to its involvement in metabolism, it controls the physical and psychological responses to environmental stimuli, especially those with emotional content [30, 31]. Together with the hypothalamus, the amygdala produces autonomic components of feelings and is responsible for mediating all emotional responses and influences homeostatic mechanisms and neuroendocrine signaling [32].

Moreover, the anatomical proximity between the hippocampus and the amygdala facilitates the efficient processing of information related to stress. It alters the processing of emotionally salient stimuli that triggers responses through the hypothalamic-pituitary-adrenal (HPA) and other effector systems [33], see **Fig. 1**). In several imaging studies, the amygdala mediates emotional reactions that modulate fear and anxiety behavior [34, 35, 36]. As an integrative detective center for emotion, the hippocampus likewise plays an essential role in forming new memories and expressing adaptive emotional behaviors. The critical function of fear and anxiety acts as a signal of threat or motivational conflict and thus triggers appropriate adaptive responses. Craig and colleagues [37] underscore that anxiety is a generalized reaction to an unknown threat or internal conflict.

Alternatively, fear is a reaction to a known external threat, which implies a different mechanism within the

nervous system [38]. Evidence suggests that this mechanism is mediated by a network of subcortical structures centered in the amygdala. Moreover, the amygdala also processes emotional arousal responses and plays a vital role in memory and motivation [15, 17]. Consistent with this view, some ablation and fear extinction studies showed that the amygdala is directly responsible for responding to threats that contribute to feelings of anxiety [16, 39, 40]. By the same intention, they found that patients with diminished feelings following amygdala damage may reflect the elimination of the indirect consequences of amygdala activity on feelings without increasing their negative impact [41, 42].

Another comparative investigation of Feinstein et al. [43] inferred that a healthy amygdala might well usually serve to inhibit panic. Another empirical observation suggested that the hyperactive amygdala can dramatically change emotional responses such as fear and anxiety [27]. These findings presumably indicate enormous evidence that the amygdala plays an essential role in processing emotions and anxiety states. However, some studies referred to patients with amygdala damage who still can feel fear, panic, and express pain [44, 45]. From the perspective of this empirical result, numerous experimental paradigms put forward the process by which the subjects modify the expression, the experience, and the physiology of their emotions, as a form of cognitive change characterized by adjusting the meaning of an emotional stimulus [46, 47, 48].

These experimental studies, which endeavored to apply emotion regulation strategies, have made explicit that subjects can modify their emotions' behavioral expression, experience, and bodily processes [49-51].

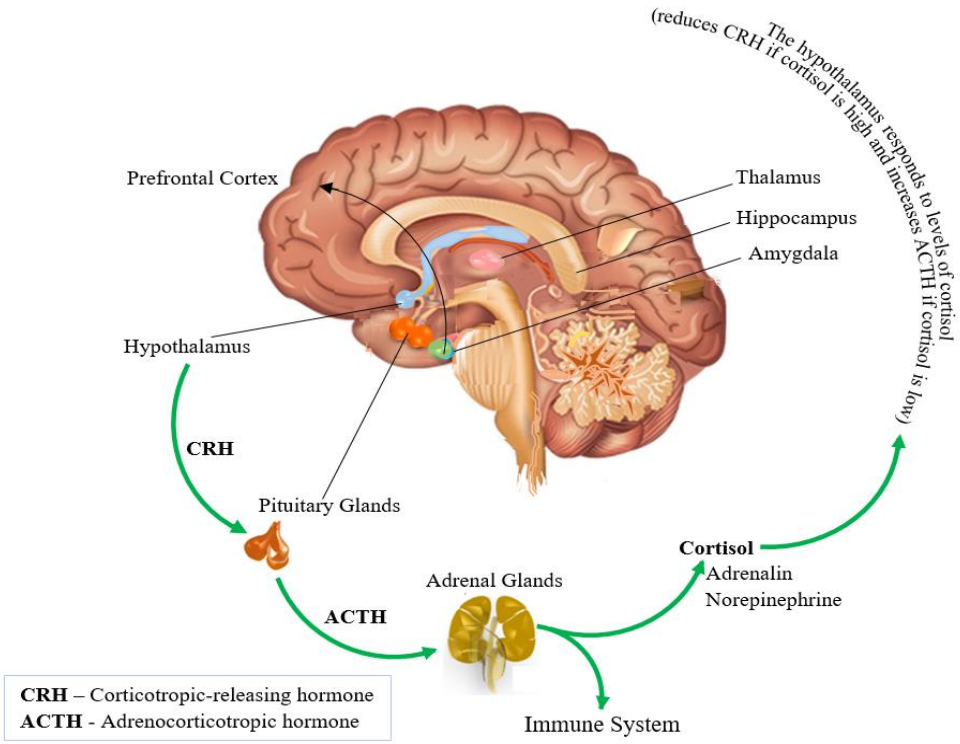

Figure 1. *Schematic of the complex neural circuitry in the brain which is responsible for stress responses and anxiety behaviors, as well as the hormonal mechanism responsible for hyperactivity of the HPA system in response to a threat and stress. A threat signal initiates the release of CRH from the hypothalamus, which is then activated by the amygdala. Through the hypothalamus, they are channelled to activate the Pituitary gland, which ultimately controls the other endocrine glands and body's hormonal response to stress. This occurs via the action of CRH that stimulates the pituitary synthesis of ACTH as an interconnecting element of the HPA Axis. In turn, ACTH travels down the bloodstream and stimulates the adrenal glands located atop of both kidneys to secrete more stress and threat hormones Adrenaline, Noradrenaline, particularly Cortisol and release them into the bloodstream to assist the body in handling stress better resulting in higher levels of cortisol in the blood. However, prolonged high cortisol levels in the bloodstream exacerbate anxiety and interfere with the body's natural self-repair mechanism. Hence, Cortisol's far-reaching, systemic effects play numerous roles in the body's effort to carry out its processes and maintain homeostasis. They are the hormones, particularly cortisol, involved in the regulation of the HPA system that plays a vital role in stress-related disorders. Correspondingly, there are sensory receptors in the brain that are deactivated when cortisol levels in the blood are high, resulting in a 'shut off' response.*

A different study observed that the amygdala is a critical component of the circuit that enables the brain to detect and respond to threats, even if it does not require the ability to experience fear [52]. The researcher added that once learned, the emotional and behavioral response occurs unconsciously and automatically. Indeed, embedded within this experience shifts, and the emotional value of a stimulus is modified. The subject is expected to have more automatic responses to match the newly acquired stimulus value [53, 54]. And in this view, physiological, cognitive, and behavioral responses may simultaneously form the experience of emotion [55]. Specific limbic system structures, the hypothalamus, amygdala, and the hippocampus, deal with the basic drives, emotions, motivations, and memory that can substantially influence the cognitive process [2, 56]. These regions work to generate and modulate fear responses to imminent and identifiable threats [57, 58]. The amygdala and the hippocampus synergize to form long-term memories of significant emotional events.

There are many processes associated with the limbic system. Still, the system is most frequently linked to emotion, and affective reactivity is believed to involve such cognitive processes that have to do with the role of a conscious effort to control innate behavior, thought, and feeling [4, 59, 60]. The essence of this impression suggests anxiety response starts in a region of the brain called the amygdala [61], where the dorsal anterior cingulate cortex (dACC) processes aversive signals and sends output to the hypothalamus, basal ganglia, and brainstem to produce defensive behaviors [62, 63]. Supplementary to this study are the inquiries making impressive claims that, although it is held that the limbic system and, in particular, the amygdala has been identified with the highest density of neuropeptides that influence the activity of the brain and the body in specific ways [58, 64, 65]. The investigation addressed that this mixture of neurotransmitters called neuropeptides travels throughout the body and the brain to support the experience of emotion through body-brain interactions [66]. Neuropeptides presumably enhance the perception of multisensory signals, and in the case of threats, the signals are suggested to reach a threshold that triggers a fear response.

3. The neural pathway that initiates the HPA axis stress response

Interestingly, high levels of neural activity are associated with the amygdala's reciprocal connections with several brain regions that would initiate physiological, behavioural, and psychological responses in various stress-related situations ([61], see **Fig. 1**). As the amygdala responds to various emotional stimuli, interacts with memory and mental state, and focuses on automatic responses such as threat detection, it plays a massive role in emotional memory and memory consolidation [64].

The brain is sensitive to various emotional stimuli, interacting with memory, state, and automatic responses such as stress detection in response to pressure and threat [66, 67]. Due to the strong emotional content involved, fear is a triggered response and is linked with the functioning of the amygdala [68]. Without the amygdala, the alarm in our brain that pushes us to avoid danger is missing [42]. The brain is the crucial organ of the anxiety response because it determines what is potentially threatening and, therefore, stressful [69]. It also regulates the behavioral and physiological responses to potentially stressful experiences. It determines how to respond emotionally using the subject's stored knowledge input. The hippocampus and the amygdala regulate the HPA axis, which mediates fight or flight response [70]. Like the rest of the brain, the hypothalamus communicates with the rest of the body through the nervous system to shift the body's energy resources towards fight or flight [71]. Tension triggers the HPA axis, a neuroendocrine system that regulates central and peripheral homeostatic adaptive responses to anxiety [72, 73]. The HPA axis regulates various bodily processes and is a vital component of the body's neuroendocrine response and behavioural changes in mediating fear and anxiety [74, 75].

When a threat is perceived, the body releases stress hormones into the bloodstream. These are complex chemicals that convey messages throughout the body via the bloodstream and trigger specific anxiety responses (**Fig. 1**). The hypothalamus triggers the pituitary gland, which causes secretion and synthesis of another hormone called corticotrophin-releasing hormone (CRH), which enables the body to resist the stress or threat until homeostasis returns [76, 77]. As outlined in **Fig. 2**, the CRH circuit stimulates the pituitary gland to secrete adrenocorticotropic hormone (ACTH) into the bloodstream. The anterior pituitary gland controls the secretion of ACTH in response to CRH from the hypothalamus. Adrenocortical secretion ACTH stimulates the adrenal cortex to release cortisol and other hormones under the control of the anterior pituitary gland. During any stressful situation, of such as injury, low blood sugar levels, and exercise, the hypothalamus secretes a releasing hormone that triggers the pituitary to release ACTH [76, 78]. The

The adrenal gland receptors detect high levels of ACTH, which also stimulate cortisol secretion. Often called the stress hormone, cortisol regulates energy-controlling blood sugar levels, mobilizes energy to target tissues and muscles, and reduces inflammation in the body. Cortisol concentration plays a vital role in the body's stress response as an indicator of stress level [78, 79]. However, when cortisol levels rise, the HPA axis slows down CRH release from the hypothalamus and ACTH from the pituitary gland, as shown in **Fig. 2**. As an adaptive response to a threat, the level of various hormones also changes. When threats or stress are high, cortisol secretion increases as well.

Correspondingly, the ACTH levels start to fall when cortisol is high. As shown in **Fig. 2**, the end-product of the HPA axis is cortisol and other stress hormones, norepinephrine and epinephrine, which contribute to the inflammatory response. Cortisol, an essential glucocorticoid, has many significant functions in the body's natural processes, regulating metabolism, immune response, and general homeostasis [80, 81]. Cortisol potentiates the body into a general state of arousal, giving hyperactive and overwhelming influences on the affect [82, 83]. To foster physiological response, cortisol taps into proteins stored in the liver provides the body with high amounts of glucose in the bloodstream, enhances the brain's use of glucose, and increases the availability of substances that repair tissues, reducing inflammation [84, 85, 86].

4. Neurochemical mechanism underlying GABAergic synaptic plasticity

Stress exposure increases the release of amygdala neurotransmitters, including glutamate, GABA, noradrenaline, and serotonin. This immediately activates a signal transduction pathway with a downstream molecular cascade that strengthens postsynaptic neurons, resulting in the instant regulation of specific genes engaged in neuroplasticity processes. The nervous system coordinates all organ system functions down to the primary functional unit - the neuron through positive and negative feedback loops [87, 88]. Every behavior, emotion, and the essential features of living interact in fundamental ways in the entire brain. How neurons behave concerning emotions ultimately implicates a central state of emotion, like fear and anxiety.

The HPA axis integrates the neuroendocrine functions and regulates hormonal and neurotransmitter release, particularly the γ-aminobutyric acid (GABA) neurotransmitter systems, to innervate the effect of adrenocortical responses of stress and anxiety-associated brain [89, 90, 91]. Conventional neurotransmitters can either be inhibitory or excitatory and released by the presynaptic axon terminal into the synapse upon stimulation with specific receptors. The chief inhibitory neurotransmitter is GABA, while

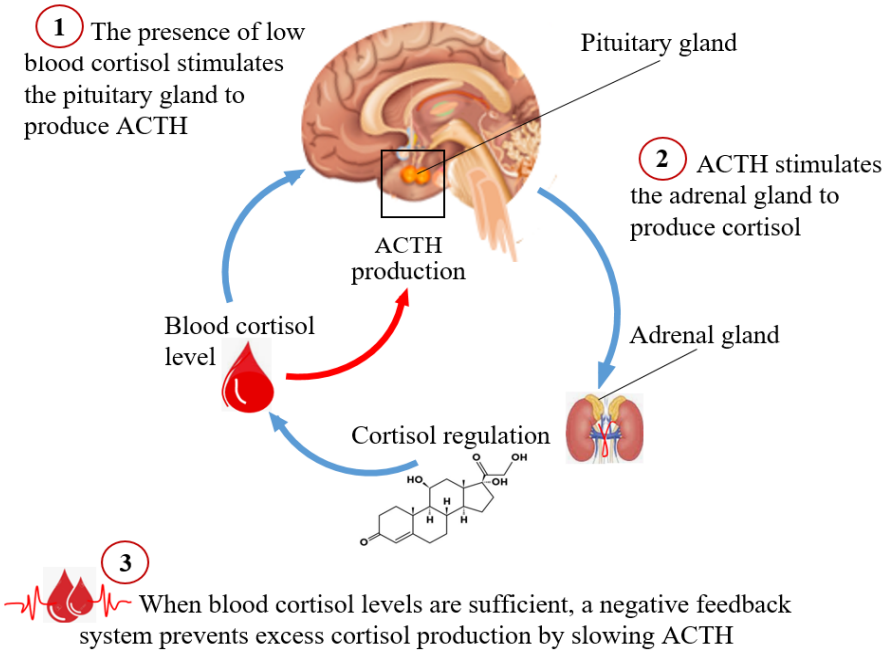

Figure 2. *Elucidates the regulated function of HPA axis stress response that induce the pituitary gland to release ACTH into the bloodstream. This subsequently reaches the adrenal gland and leads to secretion of cortisol hormone. In a negative feedback loop, sufficient cortisol inhibits the release of both ACTH and CRH. A positive and negative feedback loop helps keep cortisol levels within a healthy range.*

glutamate is the main excitatory neurotransmitter in the CNS [92, 93]. GABA, an amino acid produced naturally in the brain, functions as the principal inhibitory neurotransmitter because it inhibits specific brain signals and slows down the flow of information, thus reducing the nervous system's activity [94, 95, 96]. When one is anxious, over-reactive fear circuits are coursing from the lateral and central nucleus of the amygdala.

Increasing GABA at the neuronal synapse inhibits the neuron's action potential generation, making it less likely to excite nearby neurons. Moderating the extent to which the GABA neurotransmitters connected to the central nucleus of the amygdala are hence adequately positioned via synapses encourages synaptic inhibition [95, 96]. As illustrated in **Fig. 3**, these synapses are tiny gaps filled with ions where neural signals are communicated between neurons (axon and dendrites) via neurotransmitters. These neurotransmitters are molecules that travel from one neuron to another neuron to allow chemical transmission. They cross a synapse between them to communicate, as shown in **Fig. 3**. Upon activation, the messages they send are believed to play a role in anxiety regulation. GABA and its receptor activation can cause a massive increase in chloride conductance through the cell membrane [97, 98]. This facilitates a regulatory role in maintaining a balance between neuronal excitation and inhibition.

When GABA molecules release into the synaptic cleft, they attach to a protein in the brain and bind to their receptors. It functions to inhibit or reduce the neuronal activity of the neurons by inhibiting nerve transmission, thereby reducing unwanted brain excitability. This ultimately produces a calming effect, helps balance the body, and maintains homeostatic adaptive responses to anxiety [92, 94].

A synapse is a site of functional contact between neurons that facilitate the transmission of impulses from one (presynaptic) neuron to another (postsynaptic) neuron. Typically, when GABA binds to a protein – known as $GABA_A$ receptors and opens up the chloride ion channels causing depolarization and thus decreasing cellular excitability by inhibiting nerve transmission. However, GABA is not the only molecule that can change this channel receptor's opening. The mechanism underlying this effect virtually blocks specific brain signals to reduce amygdala hyperactivity and prevent inappropriate emotional and anxious responses [99, 100]. Current studies claim that the GABA neurotransmitter being released reduces anxiety. It is their natural function to reduce the activity of the neurons to which it binds. Some studies suggest that endogenous GABA helps control fear and anxiety when neurons become overexcited. GABA plays a vital role in behaviour and cognition, and its inhibitory interneurons represent a promising therapeutic target for the treatment of anxiety disorders.

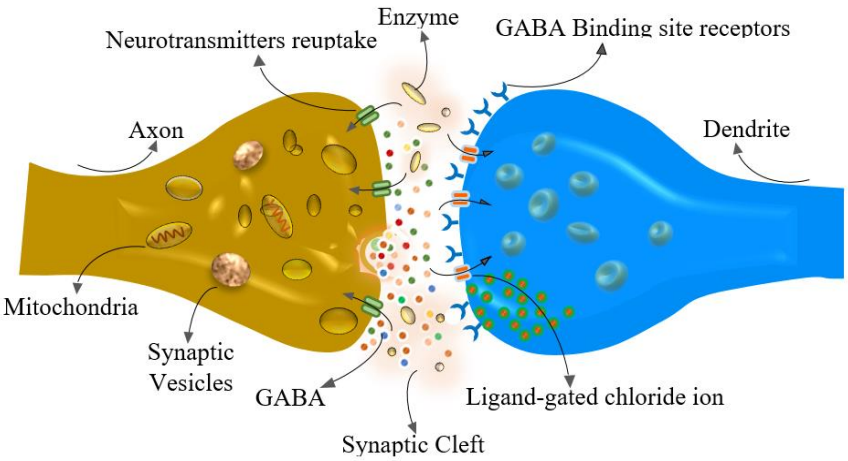

Figure 3. *In the amygdala, GABA interneurons function as inhibitory neurons for transmitting neural information between each synapse. GABA has a structure of amino acids and neurotransmitters stored in synaptic vesicles positioned along the presynaptic membrane to enhance molecular secretion to modulate stress responses. When a neural message reaches the axon terminal, GABA neurotransmitter is released, carrying information across the synaptic gap to the receiving neuron (dendrite). The essence of this GABA plays a vital role in reducing overwhelming feelings of anxiety by slowing down the signals or neuronal excitability throughout the nervous system.*

5. Amygdala's role in regulating the negative feedback effect of cortisol on adrenocortical responses

Stress activation is believed to be mediated by glucocorticoid cortisol at the level of the amygdala via feed-forward mechanisms [100]. The amygdala is highly involved in the emotional reactions when danger is perceived as a distress signal to the hypothalamus, which stimulates the sympathetic nervous system and triggers a cascade of hormones resulting in the final release of cortisol from the adrenal cortex situated atop the kidney [101-103]. Risks seem to be linked to the HPA axis, releasing stress hormones abnormally [104]. It causes anxiety and depression and affects the digestion, immune system, mood and emotions, sexuality, and energy storage and use because the HPA axis involves these complex functions [105]. Most body cells have cortisol affect many tissues in the body [102,106]. In this regard, the manifestation of the HPA axis transect with those of both anxiety dysfunction is caused by tension and anxiety.

Healthy body functioning can be disrupted when cortisol is released in excess due to prolonged activation of stress response systems in the body and brain. So when a high amount of cortisol interacts with the hypothalamus, the HPA axis will slow down its activity to maintain hormonal balance within appropriate levels [103]. In the presence of circulating hormonal factors, cortisol and other stress hormones via the bloodstream to relevant organs mobilize the body's resources by increasing energy and decreasing inflammation, especially in injuries. These systems-level physiological changes suggest that CRF plays an important role in developing a functional HPA axis and is a major integrator of adaptive responses in mediating anxiety-related behavioural consequences [84, 98].

However, due to unrelenting anxiety, the high cortisol levels can wear down the brain's ability to function appropriately, including metabolism. Cortisol has been considered one of the main culprits in the stress-anxiety connection, although it plays a fundamental role in helping one cope with threats [107, 109]. It can be enlightening to consider that anxiety disorders involve prominent disturbances of both cognitive and emotional regions deeply interwoven in the brain's fabric that can be conceptualized as disorders of the emotional-cognitive brain [60, 108, 109, 110].

The perception of the threat depends upon the anxiety, as one perceives threats about self, the world, or related to the future. This threat perception elicits a physiologic reaction associated with rapid heartbeat, blood pressure, sweating, and an overall sense of vigilance, exacerbating the activation of the first response of flight or fight [78, 115]. In some cases, anxiety symptoms may persist even after the threat is gone. Yet, alterations in the HPA axis suggest the neurobiological basis of anxiety disorders with reported structural and functional differences that can manifest dispositional negativity across disparate psychopathologies [116, 117]. Despite the fact they are both stressful, fear is an intense physiological reaction to an immediate danger, whereas anxiety is an emotion of future threat that may occur [120, 121]. Anxiety involves the expectation of future threats, is fear-based, and may occur unexpectedly, even in the absence of real danger. Studies [122] indicated that those with heightened sensitivity to anxiety respond to those sensations with dread and a pressing urge to escape a dangerous situation. Hence, anxiety can only be understood by considering some of its cognitive traits because a primary aspect of anxiety appears to be uncertainty, which negatively affects self-esteem and leads to insecurity [123]. Thus, anxiety and insecurity are both fears of abstract threats that impede the ability to mitigate their adverse impact resulting in helplessness and isolation [77, 124]. A moderate amount of anxiety helps subjects think and act more effectively and is a normal emotion under stressful circumstances or threats. Thus, mild anxiety is adaptive and sustains motivation for survival. It is characterized by adaptive emotion that prepares one both physically and psychologically for coping with an adverse event that could be extremely stressful [118].

Although adapting is not easy, there have to be conscious efforts on the part of the executive control system necessary to bring the body and mind in tune and coherence about executing a behavior - the edgy feel vulnerable and weak between threat perceptions. Thus, the anxious often feel a sense of uncertainty and helplessness, becoming withdrawn with a distinct need for solitude [117, 125]. It is important to note that the entire process begins with negative thoughts due to stressful events and constant threats that intensify over an extended period, escalating until panic attacks set in [125]. Intrusive thoughts build up recurring concerns of risky situations involving threats and bring about the onset of anxiety and panic disorder. Symptoms are caused by feelings of extreme apprehension of impending doom that occur even in the absence of actual danger.

Adapting to anxiety involves physiological and psychological responses as a consequence, one experience a great deal of stress for what might happen

in the future such as the detrimental impact of COVID-19 pandemic affecting the global health and economy. Thus, it is always future-oriented, fear-based, and focused on worrying about what will come. Conceivably one may become excessively anxious about the need for reasonable safety precautions [114, 126, 127]. Therefore, that leads to the thinking part of anxiety, which brings dominant symptoms of nervousness, which suggests always planning, looking ahead, trying to control circumstances, and a stressful urge to defeat a threat [128, 129]. As much as anything, stress and anxiety are only a problem when they exceed legitimate concerns in a way that is unreasonable and disproportionate to the actual threat, pressure or both. Indeed, they are often engulfed in a diffuse sense of apprehension, tension and confusion, associated with an increasingly helpless and uncertain feeling.

6. Conclusion

Our review focused primarily on mapping hormonal pathways to identify specific neuronal circuits and their functions related to different brain regions and how they interacted, particularly those that initiate stress responses. Increasing brain activity studies have made significant contributions to our understanding of the brain's capacity to perceive emotional information and its role in meditating stress and anxiety-related behaviors. Cognitive and emotional functions appear closely linked when the mind, brain, and emotions work optimally.

Similarly, peripheral physiological changes can be related to multiple emotional experiences that facilitate defensive psychophysiological adaptation. In cognitive-behavioral responses to stress, these neural representations are more closely linked with parallel brain regions, and neural events are believed to be the most directly involved in developing these processes. Accordingly, we refer to brain circuits that detect and respond to threats as physiologically self-protective functions, towards behavioural expressions in avoiding threats as defensive behaviours. As a result of the amygdala activation, there is a significant interaction with the cortical region, which profoundly impacts cognitive and emotional functions, dynamically affecting the mental state. We focused on understanding how the HPA stress and anxiety response pathway and the amygdala activation influence the circuitry that mediates adaptive or defensive and pathological anxiety behaviors to address these essential considerations.

Various studies provide significant insight into why the emotional centers can seem out of control, particularly if they are constantly alerted to threats and stress, which could explain how amygdala damage can occur. The cortex is similarly equipped with a mechanism for processing emotional information, which filters out and controls the emotional input it receives from the amygdala. This is expected because the amygdala's proximity to the cortex contributes to the connection between emotions and cognition. The HPA, the amygdala, and the prefrontal cortex help manipulate adaptive success.

The brain’s major function is to regulate the activity of various body systems and how neurons respond to emotions. In this respect, we attempted to elucidate whether the *neurochemical mechanism* involved in GABA molecules in brain circuits relevant to stress-response processes could provide valuable information regarding the psychobiology of stress and anxiety and its reducing effects. GABAergic interneurons are believed to compose amygdala circuits, and this neurotransmitter plays a significant role in normal and abnormal stress responses.

Conflict of Interest

The authors declare no conflict of interest

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