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Mini-review

A COMPARATIVE ANALYSIS OF NEUROHUMORAL REGULATION AND HORMONAL DYNAMICS IN POST-TRAUMATIC STRESS DISORDER (PTSD) BETWEEN HUMAN AND MOUSE MODELS

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Abstract:

Post-traumatic stress disorder (PTSD) is a multifaceted psychiatric condition arising from exposure to traumatic events, affecting millions globally, particularly among veterans, survivors of violence, and individuals impacted by natural disasters. It manifests through persistent symptoms such as intrusive memories, hyperarousal, emotional dysregulation, and cognitive impairments. This review examines the neurobiological mechanisms underlying PTSD, focusing on the critical roles of neurohumoral regulation and hormonal dynamics, particularly the hypothalamic-pituitary-adrenal (HPA) axis. Dysregulation of the HPA axis, characterized by paradoxical cortisol dynamics that transition from hyperactivity in acute stress phases to hypoactivity in chronic stages, is a hallmark of PTSD. This hormonal imbalance influences the neural pathways associated with fear responses, emotional regulation, and stress recovery.

Additionally, the review highlights the complex interplay between the HPA axis and other hormonal systems, such as the hypothalamic-pituitary-thyroid (HPT) and hypothalamic-pituitary-gonadal (HPG) axes, and neuropeptides like oxytocin and vasopressin. These interactions contribute to the disorder's heterogeneity and individualized responses to trauma. Animal studies, particularly those using mouse models, have provided critical insights into genetic, physiological, and methodological factors influencing PTSD development. However, notable differences in glucocorticoid dynamics, receptor sensitivity, and stress recovery between humans and mice underscore the challenges of directly extrapolating findings across species.

Furthermore, the review explores sex-specific vulnerabilities, with women being disproportionately affected due to the modulatory effects of estrogen, progesterone, and testosterone on stress resilience and emotional processing. Neurochemical dysregulation, particularly involving serotonin, dopamine, and gamma-aminobutyric acid (GABA), further compounds the complexity of PTSD, influencing mood regulation and behavioral responses to trauma.

This comprehensive analysis underscores the need for a multidimensional approach to understanding PTSD, integrating hormonal, genetic, and neurochemical perspectives. Such an approach is vital for developing targeted therapeutic interventions that address the dynamic and individualized nature of the disorder.

Keywords: Post-traumatic stress disorder, neurohumoral regulation, HPA axis, hormonal dynamics, neuropeptides, sex hormones, stress response, interspecies differences, mouse model.

1. INTRODUCTION

Post-traumatic stress disorder (PTSD) is a complex psychiatric condition that arises following exposure to traumatic events. It is characterized by persistent symptoms, including intrusive

memories, hyperarousal and emotional numbing. PTSD is a prevalent condition, affecting millions of individuals globally, particularly among veterans, survivors of violence, and victims of natural disasters. A comprehensive understanding of the neurobiological underpinnings of PTSD is essential for the development of effective therapeutic interventions (Bryant, 2019; Yehuda et al., 2021).

Recent advances in research have highlighted the importance of neurohumoral regulation and hormonal dynamics in the pathophysiology of PTSD. The hypothalamic-pituitary-adrenal (HPA) axis plays a pivotal role in the stress response, and dysregulation of this axis is a common feature of individuals with PTSD (D'Elia et al., 2021; von Majewski et al., 2023). Such dysregulation may result in aberrant cortisol levels and disrupted feedback mechanisms, thereby exacerbating the symptoms associated with the disorder. Moreover, neurotransmitter systems, including those involving serotonin, dopamine, and gamma-aminobutyric acid (GABA), interact with hormonal pathways, thereby influencing emotional regulation and behavioral responses to stress (Narvaes & Martins de Almeida, 2014; Bremner & Pearce, 2016).

Animal research, particularly studies using mouse models, has been instrumental in understanding PTSD's neurobiological foundations (Goswami et al., 2013; Lisieski et al., 2018). These models permit the controlled investigation of genetic and environmental factors that contribute to stress responses and the symptomatology of PTSD. It is noteworthy that the single prolonged stress (SPS) model has been extensively utilized to simulate PTSD-like behaviors in mice, thereby providing insights into the biological processes that underlie the disorder (Lisieski et al., 2018). However, researchers must carefully consider the limitations of translating findings from animal studies to human experiences.

This review aims to critically examine the neurobiological regulation of PTSD across human and mouse models. By comparing genetic, physiological, and methodological variations, the research seeks to bridge the gap between laboratory discoveries and clinical treatments. Understanding these nuanced differences is crucial for developing more effective therapeutic approaches and comprehending the complex nature of PTSD.

2. HORMONAL SYSTEMS IN PTSD

2.1. Hypothalamic-Pituitary-Adrenal (HPA) axis

Role in Stress Response and PTSD Development

The hypothalamic-pituitary-adrenal (HPA) axis plays a central role in the body's response to stress. When exposed to a stressor, the hypothalamus releases corticotropin-releasing hormone (CRH), which stimulates the anterior pituitary to secrete adrenocorticotropic hormone (ACTH). ACTH then stimulates the adrenal glands to produce glucocorticoids (D'Elia et al, 2021; Algamal, 2018). Dysregulation of the HPA axis has been implicated in the development of post-traumatic stress disorder (PTSD). Clinical research has revealed a nuanced pattern of cortisol dysregulation that significantly impacts the neurobiological mechanisms underlying PTSD symptomatology (Cranston, 2014; Algamal et al., 2018; D'Elia et al., 2021; Fischer et al., 2021; Lee et al., 2022).

Studies have demonstrated that individuals with PTSD often exhibit altered cortisol levels, including hypocortisolism and heightened sensitivity to negative feedback mechanisms, which can exacerbate symptoms such as anxiety and hyperarousal (Algamal et al., 2018; D'Elia et al., 2021; Fischer et al., 2021; Lee et al., 2022). According to these researchers, the observed cortisol reduction potentially represents a neurobiological adaptive mechanism designed to mitigate potential neurotoxic consequences of prolonged stress hormone exposure (D'Elia et al., 2021; Fischer et al., 2021; Lee et al., 2022). However, there is an inherent contradiction in the literature, as there are findings that prolonged exposure to cortisol can alter the regulatory systems of the HPA axis, thereby contributing to the development and maintenance of PTSD (Cranston, 2014). It is presumed that, in the early stages of traumatic stress, cortisol can be elevated, which contributes to the

development of PTSD through neurotoxicity and effects on brain structures. In the long term, however, develop hypo reactivity of the HPA system, resulting to insufficient cortisol production.

There are probably two stages in the dynamics of cortisol that contribute to the development of PTSD:

Early Traumatic Stress Phase: During the initial stages of traumatic exposure, cortisol levels typically become significantly elevated. This hormonal surge can contribute to PTSD development through direct neurotoxic effects and structural alterations in critical brain regions. The heightened cortisol environment creates a neurobiological vulnerability that may predispose individuals to long-term psychological consequences.

Chronic Stress Phase: As the stress response becomes prolonged, individuals often develop hypo-reactivity within the HPA system. This adaptation manifests as insufficient cortisol production, representing a fundamental shift in the body's stress response mechanisms. The transition from hypercortisolism to hypocortisolism highlights the dynamic and adaptive nature of the human stress response system.

This paradoxical cortisol dynamics underscore the complexity of PTSD's neurobiological foundations.

Recent scientific research has provided compelling evidence that genetic factors also play a significant role in an individual's susceptibility to PTSD. Specific gene variations can influence an individual's neurobiological stress response, potentially increasing the risk of PTSD. Several genes have been identified as critical in the development of PTSD, including FKBP5 (FK506 binding protein 5), NR3C1 (nuclear receptor subfamily 3 group C member), CRHR1 (corticotropin-releasing hormone receptor 1) and CRHR2 (corticotropin-releasing hormone receptor 2). These genetic polymorphisms can modulate an individual's stress response mechanisms, potentially creating a predisposition to developing PTSD following traumatic experiences (Carvalho et al., 2017; Sheerin et al., 2020).

Additionally, the hypothalamus integrates physiological aspects of stress response through connections with the prefrontal cortex, amygdala, and hippocampus, potentially influencing PTSD pathophysiology through various pathways beyond the HPA axis (Raise-Abdullahi et al., 2023). The hypothalamus has also been shown to play a variety of roles in the development of PTSD via the hypothalamic-pituitary-thyroid (HPT) and hypothalamic-pituitary-gonadal (HPG) axes, and by secreting growth hormone, prolactin, dopamine and oxytocin (Raise-Abdullahi et al., 2023). The following subsections describe these systems in more detail.

It can be stated that the HPA axis represents a fundamental component of the stress response, with its dysregulation contributing significantly to the pathophysiology of PTSD. The complex mechanisms underlying PTSD are further highlighted by altered cortisol dynamics, genetic predispositions and the interplay of the hypothalamus with other brain regions and hormonal pathways. Beyond the HPA axis, alternative pathways such as the HPT and HPG axes, alongside other hypothalamic hormones, contribute to the disorder's development, emphasizing the multifaceted nature of stress-related pathologies. Therefore, it is of great importance to study the detailed mechanisms of its involvement in the regulation of this disease.

Comparison of HPA Dysregulation in Humans and Mice

Humans and mice share the same basic components of the HPA axis: the hypothalamus releases CRH (Venihaki & Majzoub, 2002); the pituitary gland releases ACTH in response to CRH; the adrenal glands produce glucocorticoids (cortisol in humans, corticosterone in mice) (D'Elia et al., 2021; Algamal, 2018). In both species, the HPA axis responds to stressors by activating this cascade, increasing glucocorticoid production to mobilize energy, suppress inflammation and enhance survival mechanisms (Venihaki & Majzoub, 2002).

Both humans and mice exhibit HPA dysregulation under chronic stress or PTSD, but the mechanisms and outcomes differ due to physiological, genetic and neurobiological factors (Table 1 details the differences).

While mouse models provide critical insights into HPA dysregulation and PTSD mechanisms, differences in glucocorticoid dynamics, receptor sensitivity, and recovery rates between humans and mice highlight the need for caution in direct extrapolation.

Table 1. Key differences in human and mouse HPA dysregulation

Aspect	Humans	Mice	References
Glucocorticoid type	Cortisol is the primary glucocorticoid	Corticosterone is the primary glucocorticoid	(D'Elia et al., 2021; Algamal, 2018)
Basal levels	Humans have diurnal variations, with higher levels in the morning and lower at night	Similar diurnal rhythm, but corticosterone peaks at the start of the active phase (evening for nocturnal mice)	(Spiga et al., 2011; Dickmeis, 2009).
Receptor sensitivity	Glucocorticoid receptor (GR) and mineralocorticoid receptor (MR) sensitivity vary, with MR being more active at baseline	Mice show species-specific GR/MR activity, with some differences in brain region distribution	(Pryce, 2008; Meijer et al., 2019)
Stress recovery	HPA recovery may be slower in humans, especially in chronic stress or PTSD	Mice tend to have a faster stress recovery, but this varies across strains	(Anisman et al., 1998; Porcu & Morrow, 2014; García et al., 2019)
PTSD and Chronic Stress	Chronic stress and PTSD can lead to both hypoactivity (low cortisol) and hyperactivity (high cortisol) of the HPA axis, depending on the stage of the disorder* and the presence of comorbid conditions**	Chronic stress in mice often leads to hyperactivation of the HPA axis, unless genetically predisposed to hypoactivity. The mouse model of single prolonged stress (SPS) shows suppression of the stress-induced corticosterone response	(Cranston, 2014; Dekel et al., 2017; D'Elia et al., 2021; Lee et al., 2022; Zhu et al., 2014; Perrine et al., 2016; Souza et al., 2017; Borrow et al., 2019)
Sex Differences	Women are more likely to show HPA dysregulation in disorders like PTSD	Mice also exhibit sex differences, but these depend heavily on strain and experimental conditions	Bangasser& Valentino, 2014; Pooley et al., 2018

*Research suggests that people with PTSD often have inconsistencies in their cortisol levels, which can manifest as either hypercortisolism during acute stress responses or hypocortisolism in chronic stages. For example, PTSD patients may have lower basal cortisol levels than healthy controls, particularly when dissociative symptoms are present, suggesting HPA axis hypoactivity. Conversely, some individuals may have elevated cortisol levels during trauma activation or stress reminders, reflecting HPA hyperactivity. The stage of PTSD also plays a crucial role in determining whether an individual experiences HPA hypoactivity or hyperactivity. Acute phases following trauma may trigger heightened cortisol responses, while chronic exposure to stressors can lead to a dampened HPA response characterized by lower cortisol levels (Lee et al., 2022).

**The presence of comorbid conditions such as depression can further complicate cortisol dynamics. Individuals with comorbid PTSD and depression may exhibit higher baseline cortisol levels and altered responses to stress compared to those with PTSD alone. This suggests that the hormonal response in PTSD is not uniform and can vary significantly based on individual circumstances and accompanying psychological conditions (Dekel et al., 2017).

These models are invaluable for understanding stress-related neurobiology, but results must be contextualized within a species-specific framework.

2.2 Sympathetic-Adrenomedullary System (SAM) in PTSD

Contribution of Catecholamines (e.g., Adrenaline, Noradrenaline)

The sympathetic-adrenomedullary system (SAM) is activated during periods of stress, resulting in the release of catecholamines, including adrenaline and noradrenaline. These hormones prepare the body for a "fight or flight" response, increasing heart rate, blood pressure, and energy availability. In individuals diagnosed with PTSD, elevated catecholamine levels have been linked to increased arousal and the onset of anxiety symptoms (Pace & Heim, 2011; Algamal et al., 2018). In particular, individuals diagnosed with PTSD tend to produce elevated levels of norepinephrine in response to stressful stimuli. The magnitude of this hormone release is frequently associated with the severity of their symptoms (Algamal et al., 2018; von Majewski et al., 2023). Furthermore, research indicates that post-traumatic stress disorder is associated with both alterations in the SAM system and the HPA axis, which may contribute to the development of comorbid somatic conditions and immune dysregulation (Rohleder & Karl, 2006; Pace & Heim, 2011). Patients with PTSD display elevated levels of inflammatory markers, diminished natural killer cell activity, and altered T lymphocyte counts (Pace & Heim, 2011).

Key Differences in Catecholaminergic Responses in Humans vs. Mice

Although both species demonstrate elevated catecholamine responses to stress, the duration and intensity of these responses exhibit notable discrepancies. Chronic exposure to stress in humans has been linked to sustained elevations in catecholamines, which can contribute to the development of anxiety disorders. In contrast, studies on rodents indicate that although initial catecholamine spikes are substantial, they may not persist as long-term adaptations occur (Souza et al., 2017). Additionally, noradrenergic receptor distribution in the hippocampus differs between rodents and humans, potentially affecting drug responses (Szot, 2006). It is therefore imperative to gain a deeper understanding of these differences if we are to develop effective treatments for PTSD that target the SAM system.

2.3 Sex hormones and PTSD

Sex hormones play a crucial role in understanding the complex dynamics of PTSD. Research suggests that women are twice as likely as men to develop PTSD, with sex hormones playing a critical role in this disparity (Ney et al., 2019; Ravi et al., 2019; Mendoza et al., 2016; Pivac, 2019). Progesterone in particular may enhance emotional memory consolidation during trauma, potentially increasing vulnerability to PTSD in women, particularly during the mid-luteal phase of the menstrual cycle (Ney et al., 2019). Estradiol, progesterone and allopregnanolone influence fear psychophysiology and stress axis regulation, which are critical for PTSD development (Ravi et al., 2019; Pivac, 2019). Interestingly, sex differences in the locus coeruleus-norepinephrine system and its regulation by stress hormones may also contribute to increased arousal in women (Bangasser et al., 2016). In addition, sex hormones may have neuroprotective effects by reducing neuroinflammation following severe stress exposure, which may influence susceptibility or resilience to trauma (Mendoza et al., 2016). Estrogen has been shown to exert neuroprotective effects (D'Elia et al., 2021). Conversely, testosterone modulates aggressive and risk-taking behaviors associated with trauma exposure (von Majewski et al., 2023). Although testosterone may modulate aggressive behaviors associated with trauma, it does not directly lead to a risk of PTSD. The relationship between sex hormones and PTSD is complex.

Inflammatory responses also differ between the sexes, with men having higher levels of pro-inflammatory cytokines, which may have a protective effect against persistent PTSD. Interestingly, estradiol levels in men may further modulate this protective mechanism (Lalonde et al., 2021).

Variability in Sex Hormone Modulation Between Species

Variability in Sex Hormone Modulation Between Species

Exploration of the role of sex hormones in post-traumatic stress disorder reveals parallels and differences between humans and mice, highlighting the complexity of neurobiological stress responses. In both species, estrogen exhibits neuroprotective properties, reducing neuroinflammation and potentially modulating stress resilience (Mendoza et al., 2016; D'Elia et al., 2021). Similar protective mechanisms may not be as pronounced in female rodents due to differences in hormonal regulation and receptor sensitivity (Algamal et al., 2018). The effects of testosterone are more divergent: in mice, it primarily affects aggressive behavior and risk assessment (Rieger et al., 2018), whereas in humans it more subtly moderates trauma-related behavioral responses (von Majewski et al., 2023). Notably, sex differences in the locus coeruleus-norepinephrine system show similarities across species, with both mice and humans exhibiting distinct hormonal regulation of stress arousal (Bangasser et al., 2016). Inflammatory responses also show species-specific differences, with males showing different pro-inflammatory cytokine patterns compared to mice (Hodes et al., 2021), suggesting that while basic neurobiological mechanisms are common, the precise manifestation of hormonal effects on PTSD differs between humans and animal models. Future interdisciplinary research must continue to fill these gaps.

2.4 Other hormonal systems

Thyroid Hormones and Their Role in PTSD Pathophysiology

Thyroid hormones have been implicated in mood regulation and cognitive function. Alterations in thyroid hormone levels have been observed in individuals with PTSD, suggesting a possible link between thyroid function and stress-related disorders (D'Elia et al., 2021). Studies have found elevated levels of triiodothyronine (T3) in individuals with PTSD (Wang et al., 1995; Toloza et al., 2020). A meta-analysis found higher levels of free T3 and total T3 in PTSD patients, particularly those with combat-related PTSD (Toloza et al., 2020). Positive correlations were found between T3, T4 and hyperarousal symptoms in combat veterans (Wang et al., 1995). Furthermore, a large longitudinal study found that PTSD symptoms were associated with an increased risk of hypothyroidism in women, following a dose-dependent pattern (Jung et al., 2018). In mice, adult-onset hypothyroidism produced mild anxiety-like behaviors, which were reversed by T3 or thyroxine (T4) supplementation (Buras et al., 2014). These findings suggest that thyroid dysfunction may play a role in the pathophysiology of PTSD, although more research is needed to fully understand this relationship.

Involvement of Oxytocin and Vasopressin in Emotional Regulation and Stress Responses

Oxytocin and vasopressin are neuropeptides involved in social bonding and emotional regulation. Recent studies have investigated the involvement of oxytocin (OT) and vasopressin (AVP) in PTSD. Male patients with PTSD showed lower basal salivary OT levels compared to healthy controls (Frijling et al., 2015). Human research has also suggested that oxytocin may have anxiolytic effects and may alleviate some symptoms of PTSD by promoting social support behaviors (von Majewski et al., 2023). Conversely, vasopressin has been associated with increased anxious behaviors under stressful conditions. The balance between these neuropeptides may influence how individuals process trauma and respond emotionally (Algamal et al., 2018).

In mice, both OT and AVP effectively reduced isolation-induced hyperaggression, with the antiaggressive effects of OT mediated primarily through V1a receptors (Tan et al., 2019). Intranasal OT administration improved fear extinction retrieval in a rodent model of PTSD and reversed stress-induced increases in brain and plasma pro-inflammatory cytokines (Wang et al., 2018). These

findings highlight the potential therapeutic role of OT in PTSD, affecting both behavioral and neuroinflammatory profiles.

3. NEUROHUMORAL MECHANISMS IN PTSD

Interaction Between Hormonal Systems and Neurotransmitters

Neurotransmitters such as serotonin, dopamine and gamma-aminobutyric acid (GABA) are integral to the regulation of mood and the response to stress. In individuals with PTSD, there is frequently a disruption in the regulation of these neurotransmitters. For example, studies have shown that individuals with PTSD typically have lower serotonin levels, which can contribute to the development of depressive and anxiety disorders. This reduction in serotonin may be associated with alterations in hormonal systems, particularly the HPA axis, which can exacerbate stress responses and emotional dysregulation (Aliev et al., 2020).

Dopamine is another critical neurotransmitter, involved in reward processing and motivation. Dysregulation of dopaminergic pathways has been linked to the hyperarousal and avoidance behaviors frequently observed in PTSD patients. The available evidence suggests that elevated dopamine activity may be associated with increased anxiety and stress responses following traumatic experiences (Invernizzi et al., 2023).

GABA, the primary inhibitory neurotransmitter, plays a pivotal role in regulating neural activity. In individuals with PTSD, a reduction in GABAergic function can result in heightened excitability of neural circuits associated with fear responses. This imbalance between excitatory and inhibitory signaling may be influenced by hormonal changes, particularly fluctuations in cortisol levels due to HPA axis dysregulation (Voigt et al., 2024).

Cross-species similarities and differences

While many neurotransmitter-hormone interactions are conserved across species, there are notable differences between humans and animal models such as mice. For example, studies have shown that chronic stress can lead to different patterns of neurotransmitter changes in rodents compared to humans. In mice, stress often leads to increased dopamine release, whereas in humans, chronic stress can lead to a more complex interplay involving both dopamine and serotonin systems (Aliev et al., 2020; Invernizzi et al., 2023).

CONCLUSIONS

An in-depth study of post-traumatic stress disorder (PTSD) reveals a sophisticated interplay of neurobiological mechanisms that goes beyond simple linear processes. The findings shed light on the complex interactions between hormonal systems, neurotransmitters and genetic factors that shape the pathophysiology of PTSD. The research highlights the multifaceted nature of the disorder and shows that PTSD is not a homogeneous condition, but rather a dynamic and individualized neurobiological response to trauma.

Several key findings emerge from this research:

Hormonal complexity: The HPA axis exhibits a paradoxical response to stress, shifting from initial hyperactivity to potential hypoactivity in chronic stages. This nuanced hormonal dynamic challenges simplistic interpretations of stress responses.

Interspecies variation: While animal models, particularly mouse studies, provide valuable insights, direct extrapolation to the human experience remains challenging. There are significant differences between species in hormonal regulation, receptor sensitivity and stress recovery mechanisms.

Sex-specific vulnerabilities: Sex hormones play a crucial role in PTSD susceptibility, with women twice as likely to develop the disorder. The interaction of estrogen, progesterone and testosterone creates a complex landscape of neurobiological resilience and vulnerability.

Neurochemical dysregulation: Neurotransmitter systems, including serotonin, dopamine and GABA, interact dynamically with hormonal pathways to influence emotional regulation and stress responses.

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Абрат Олександра. Порівняльний аналіз нейрогуморальної регуляції та гормональної динаміки при посттравматичному стресовому розладі (ПТСР) у людей та мишей. *Журнал Прикарпатського національного університету імені Василя Стефаника. Біологія*, **11** (2024), С33–С43.

Анотація

Посттравматичний стресовий розлад (ПТСР) — це багатогранний психоемоційний стан, що виникає внаслідок впливу травматичних подій і вражає мільйони людей у всьому світі, зокрема ветеранів, жертв насильства та осіб, які постраждали від природних катастроф. ПТСР проявляється стійкими симптомами, такими як нав'язливі спогади, гіперзбудження, емоційна дисрегуляція та когнітивні порушення. У цьому огляді розглядаються нейробіологічні механізми, що лежать в основі ПТСР, з акцентом на критичну роль нейрогуморальної регуляції та гормональної динаміки, зокрема

гіпоталамо-гіпофізарно-надниркової (ГГН) осі. Дисрегуляція ГГН-осі, що характеризується парадоксальною динамікою рівня кортизолу, який змінюється від гіперактивності на ранніх етапах стресу до гіпоактивності на хронічних стадіях, є ключовою ознакою ПТСР. Ця гормональна дисфункція впливає на нейронні шляхи, пов'язані зі страхом, регуляцією емоцій та відновленням після стресу.

Додатково в огляді підкреслюється складна взаємодія між ГГН-віссю та іншими гормональними системами, такими як гіпоталамо-гіпофізарно-тиреоїдна (ГГТ) і гіпоталамо-гіпофізарно-гонадна (ГГГ) осі, а також нейропептидами, такими як окситоцин та вазопресин. Ці взаємодії формують різноманітні прояви ПТСР та індивідуалізовані відповіді на травму. Дослідження на тваринах, зокрема на моделях мишей, дозволяють отримати важливі дані про генетичні, фізіологічні та методологічні фактори розвитку ПТСР. Водночас істотні відмінності у динаміці глюкокортикоїдів, чутливості рецепторів і механізмах відновлення після стресу у людей та мишей підкреслюють труднощі прямої екстраполяції отриманих результатів.

Крім того, в огляді розглядаються статеві відмінності, адже жінки значно частіше страждають на ПТСР через модулюючий вплив естрогену, прогестерону та тестостерону на стресостійкість і емоційну обробку. Нейрохімічна дисрегуляція, зокрема за участю серотоніну, дофаміну та гамма-аміномасляної кислоти (ГАМК), ускладнює розуміння ПТСР, впливаючи на регуляцію настрою та поведінкові відповіді на травму.

Цей комплексний аналіз підкреслює необхідність багатовимірного підходу до вивчення ПТСР, що інтегрує гормональні, генетичні та нейрохімічні аспекти. Такий підхід надзвичайно важливий для створення ефективних методів лікування, які враховують складність та унікальні особливості цього розладу.

Ключові слова: Посттравматичний стресовий розлад, нейрогуморальна регуляція, ГГН-вісь, гормональна динаміка, нейропептиди, статеві гормони, стресова реакція, міжвидові відмінності, миші як модель.