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Review Article

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Impact of Extreme Temperature Exposure on Rat Behavior: A Comprehensive Review

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ABSTRACT
Heat stress represents a critical environmental and physiological challenge, with profound implications for central nervous system function and behavioral regulation. This short review consolidates recent findings on the behavioral alterations observed in rats subjected to acute hyperthermia, with an emphasis on anxiety-like behavior, emotionality, and locomotor activity. Experimental evidence from open field, elevated plus maze, and novel object recognition tests indicates that elevated ambient temperatures (typically above 42°C) induce significant anxiety-related and cognitive deficits. These changes are likely mediated by thermally induced neuroinflammation, blood–brain barrier disruption, and oxidative stress, which impair hippocampal and cortical functioning. Understanding these behavioral signatures provides a foundational framework for developing predictive models and targeted interventions against heat-induced neurological and psychological impairments.
Keywords: Behavior, rats, temperature, environment

INTRODUCTION

The abrupt and sudden changes in environmental temperature are evident throughout the globe, which can be considered a pointer to global warming over the past few decades. For experience or changes, the weather model has forecasted that global warming is causing climate patterns (Trenberth 2011). Rapid temperature shifts, commonly referred to as "temperature whiplash," are increasingly prevalent worldwide. Between 1961 and 2023, over 60% of the globe experienced more frequent and intense swings between warm and cold extremes, often occurring within five days. This trend is attributed to factors such as increased jet stream waviness and changing evaporation patterns, driven by climate change. Projections indicate that under high greenhouse gas emission scenarios, the frequency and intensity of these temperature fluctuations will continue to escalate, potentially doubling the global population's exposure by 2100 (Tan *et al.* 2023). These abrupt changes are attributed to increased jet stream waviness and changing evaporation patterns, both linked to climate change. Projections indicate that such events will intensify under high greenhouse gas emission scenarios, posing significant threats to human health, agriculture, ecosystems, and infrastructure (Le and Bae 2020). The major changes in wind flow and seasonal temperature differences, which cause these changes (Wu *et al.* 2025). It differs and varies based on place and geography. Around the world, the hot temperatures can lead to chain reactions of different changes because the ocean, climate patterns, ice and snow, plants and animals are affected by increased air temperature (Sohail *et al.* 2025). Temperature regulates the distribution of living organisms. This extreme environmental variation can be witnessed on both the higher and the lower sides of the homeostatic critical temperature. It is established that the changes in chronic exposure to the extreme environment change the metabolic activities and the homeostasis of the mammals, and these can be considered as stressful events (Huau *et al.* 2024).

When animals are stressed, they activate several behavioral and physiological responses that are collectively known as the stress response. generally, in the first line of action, the body's set temperature gets altered due to chronic exposure and causes changes in the behavior and biochemical parameters of the body (Natarajan *et al.* 2015). Hence, it is important to say that the modulation of body thermoregulatory activities that is ultimately governed by the hypothalamo-pituitary-adrenal (HPA) axis plays a very crucial role when the body is exposed to environmental stress (Hollis *et al.* 2024).

It is also evident that the environmental stimulus also alters the ionic channels and their electrical properties of the excitable cells of the body (Mahapatra *et al.* 2024). If a chloride channel is opened by the stimulus, chloride ions enter the cell, making the local; membrane potential lower than the resting membrane potential (RMP) (Vardi *et al.* 2021). This can be strongly expressed by the electrical activities of the body's autonomic nervous system (ANS) and central nervous system (CNS). Bolt et al demonstrated that brain blood flow and electrical

activity is coupled with systemic physiological changes in the body, highlighting the interconnectedness of the CNS and ANS. The study emphasizes how fluctuations in brain activity are synchronized with autonomic physiological signals, underscoring the dynamic interplay between these two systems (Bolt *et al.* 2025). Therefore, the body electrophysiology also might be found altered along with the behavioral and biochemical parameters (Wang *et al.* 2012). These can be marked in the major electrophysiological signals (e.g., electrocardiogram (ECG), electroencephalogram (EEG)) as well as the autonomic parameters such as respiration, blood flow and heart rate variability parameters. As the analogue or digital recordings and evaluation of these parameters can be done non-invasively, these can be suggested as important biomarkers for the effects of changes in environmental temperature on the mammalian body (Nkurikiyeyezu *et al.* 2018). When these electrophysiological and autonomic parameters are recorded, the tools of digital signal processing can be applied for the time domain as well as the frequency domain analysis and the changes that occur due to environmental stressors, if any, can be smartly diagnosed with the help of artificial intelligence (Mane *et al.*2023). In homoeothermic animals, the thermoregulation mechanism is very complex, including behavioral and neuronal responses, considering different control levels and interaction with different physiological processes (Suito *et al.* 2024). As we know, the thermoregulatory system's function is to preserve the stable temperature of tissues and organs to maintain core body temperature (Mota-Rojas *et al.*)2021. Hypothalamus regulates body temperature, which utilizes information from external and internal effects of the body for thermoregulatory activity (Suito *et al.* 2024). Hyperthermia can be used in cancer treatment, and the effects on cerebral blood flow, voluntary muscle activation, neurotransmitter functions, and mental functions are involved (Field *et al.*1979). Respiratory, cardiovascular, dehydration, and heat stroke can be caused due to long exposure or chronic exposure of heat (Vaneckova and Bambrick 2013).

This review provides a comprehensive analysis of key biomarkers employed to assess the onset and severity of hyperthermia in rats, encompassing physiological (body temperature, body weight), biochemical (corticosterone levels), and structural (blood–brain barrier integrity) indicators. Additionally, non-invasive behavioral parameters such as anxiety-like responses, altered emotionality, and fecal pellet output are examined as valuable markers of systemic and neural stress. By evaluating these biomarkers across acute, chronic, and control heat exposure models—including externally induced environmental heat and incubator-based hyperthermia—the review captures the multidimensional impact of thermal stress. A systematic comparison of behavioral and physiological alterations under varying thermal conditions offers insights into the complex interplay between environmental challenges and biological responses. The structure of this review is as follows: Section 1 introduces the behavioral manifestations of heat stress in rats; Section 2 presents a detailed literature review across different rat models and thermal exposure paradigms; and Section 3 provides a summary and concluding remarks, aiming to support future research and therapeutic advancements in the context of heat-induced pathophysiology.

Stress markers

Body temperature

In rodent studies investigating thermal stress, core body temperature is commonly monitored using rectal thermometry, which remains a reliable and widely adopted technique due to its simplicity and reproducibility (Mei *et al.* 2018). Typically, a probe is gently inserted into the rectum of the rat and held in a static position for approximately one minute to ensure accurate measurement (Dangarembizi *et al.* 2017). Instruments such as six-channel tele-thermometers allow for repeated, hourly measurements, enabling researchers to track thermoregulatory responses throughout the course of heat exposure. This protocol can be implemented daily to monitor physiological adaptations or stress responses over time (Cosmi *et al.* 2009). In hyperthermia studies, continuous or interval-based rectal temperature recordings are crucial for correlating thermal load with behavioral alterations, such as anxiety, lethargy, or agitation, observed during and after heat exposure (Leon *et al.* 2010). Such comparative data serve as an essential basis for analyzing the neurophysiological and behavioral impact of sustained hyperthermic conditions.

Body weight

Body weight plays a significant role in the susceptibility and response to hyperthermia in rats. Recent studies have shown that heavier rats tend to retain more metabolic heat due to their larger body mass, which can exacerbate the rise in core temperature during heat exposure (Andrade *et al.* 2023). Additionally, increased adiposity in heavier rats acts as an insulating layer, reducing heat dissipation efficiency and making them more prone to heat stress (Lee *et al.* 2022). Experimental data indicate that lighter rats are better able to regulate their body temperature through behavioral adaptations such as increased locomotion and seeking cooler environments (Chen *et al.* 2025). Conversely, heavier rats exhibit impaired thermoregulatory responses, including reduced sweating and panting rates, leading to higher mortality under hyperthermic conditions (Maskrey *et al.* 2001). Moreover, body weight influences cardiovascular strain during heat exposure, with overweight rats showing elevated heart rates and blood pressure that further compromise heat tolerance (Bhandari *et al.* 2011). These findings highlight the critical importance of considering body weight as a variable in hyperthermia studies using rodent models (Zhang *et al.* 2023).

Corticosterone level

Corticosterone is widely recognized as a reliable biomarker of heat stress in rodents due to its role as the

primary glucocorticoid hormone secreted in response to hypothalamic-pituitary-adrenal (HPA) axis activation during thermal challenges (Gong *et al.* 2015). Under hyperthermic conditions, elevated ambient temperatures induce physiological stress that stimulates corticosterone release, serving as an indicator of both acute and chronic thermal strain (Vagnerová *et al.* 2023), Recent studies have demonstrated that corticosterone levels significantly increase in rats and mice subjected to heat exposure, correlating with behavioral changes, impaired thermoregulation, and alterations in neuroendocrine signalling (Amaral *et al.* 2010) (Veening *et al.* 2004). Moreover, advancements in enzyme-linked immunosorbent assay (ELISA) sensitivity have enabled more accurate quantification of plasma and salivary corticosterone, facilitating its use as a non-invasive biomarker in stress physiology research (Hellhammer *et al.* 2009). The integration of corticosterone measurements with electrophysiological data and behavioral parameters provides a multidimensional assessment of heat stress, making it a critical tool in experimental studies investigating thermal-induced neurobiological and systemic alterations (Xie *et al.* 2011).

Blood-brain barrier

The blood-brain barrier (BBB) has emerged as a sensitive biomarker for assessing heat stress-induced neurovascular damage due to its crucial role in maintaining central nervous system (CNS) homeostasis (Kiyatkin and Sharma 2009). Under extreme thermal conditions, hyperthermia disrupts the structural and functional integrity of the BBB by increasing permeability and compromising tight junction proteins such as claudin-5 and occludin. This leads to the infiltration of peripheral inflammatory cytokines and neurotoxic substances into the brain parenchyma, exacerbating neuronal injury and neuroinflammation (Yamaguchi *et al.* 2019) (Yoneda *et al.* 2024). Recent experimental studies have shown that markers such as increased Evans blue dye extravasation, elevated serum S100β protein, and changes in brain water content serve as reliable indicators of BBB disruption during heat stress (Cao *et al.* 2022). Moreover, molecular imaging and immunohistochemistry techniques have enhanced the ability to detect subtle BBB alterations, making it a powerful biomarker in evaluating CNS responses to thermal injury (Yamaguchi *et al.* 2019). Overall, BBB breakdown not only reflects the severity of heat stress but also helps predict neurological outcomes, supporting its utility as a key biomarker in heat-related neurophysiological research (Rust *et al.* 2012).

Faecal Pellet

Faecal pellets have emerged as a valuable non-invasive biomarker for assessing heat stress in animals, reflecting physiological and metabolic alterations induced by thermal challenges (Czech *et al.* 2022). Under heat stress conditions, changes in the composition and output of fecal matter, including shifts in gut microbiota, hormone metabolites (such as glucocorticoids), and inflammatory markers, can be detected and quantified. These fecal indicators provide an integrated measure of an animal's stress response without the need for invasive sampling, making them particularly useful in both laboratory and field studies (Idris *et al.* 2024) (Ruiz-González *et al.* 2022). Recent studies highlight that fecal glucocorticoid metabolites increase significantly in heat-stressed animals, correlating with elevated core body temperature and altered behavior patterns (Lafferty *et al.* 2019). Additionally, alterations in fecal microbiota profiles under heat stress conditions have been linked to systemic inflammation and compromised gut barrier integrity ((He *et al.* 2025). Thus, fecal pellet analysis offers a promising tool for monitoring heat stress, enabling better welfare management and early detection of heat-related physiological disturbances (Grundei *et al.* 2024).

Beyond behavioral outcomes, heat stress affects other physiological systems. For instance, (Sun et al. 2015) showed that heat stress disrupts nutrient absorption in broiler chickens by altering jejunal nutrient transporter concentrations. Sharma et al. highlighted the role of endogenous histamine in modulating heat stress pathophysiology in young rats using pharmacological approaches. Furthermore, Schechter et al. (Schechter et al. 1978) demonstrated that localized heat treatment in rats slowed tumor growth and metastasis, emphasizing heat's complex biological effects.

Limitations of Traditional Rodent Anxiety and Emotionality Tests

Despite widespread use, classical anxiety paradigms such as the open-field test, EPM, and light-dark box have faced scrutiny regarding their validity and reliability. (Hernández-Arteaga and Ågmo 2023) noted that these tests often yield inconsistent and contradictory results due to confounding factors like novelty-induced exploration and general locomotor activity rather than pure anxiety states. The lack of construct and predictive validity limits their translational value for human anxiety disorders, calling for more ethologically relevant and mechanistically informative models (Rosso et al. 2022). Earlier critiques by Archer (1973) emphasized the difficulty in interpreting behavioral data, pointing out that emotionality encompasses multiple components such as fear, anxiety, and exploration, which are not easily disentangled by simple behavioral tests (Archer 1973). Walsh and Cummins (1976) similarly cautioned that the open-field test conflates multiple dimensions, including novelty response and thigmotaxis, compromising its specificity for anxiety assessment (Walsh and Cummins 1976). Bourin et al. (2007) (Bourin et al. 2007) further stressed the role of variables such as strain, sex, handling, and environmental context in shaping anxiety-related behaviors, underscoring the need for cautious interpretation (Figure 1).

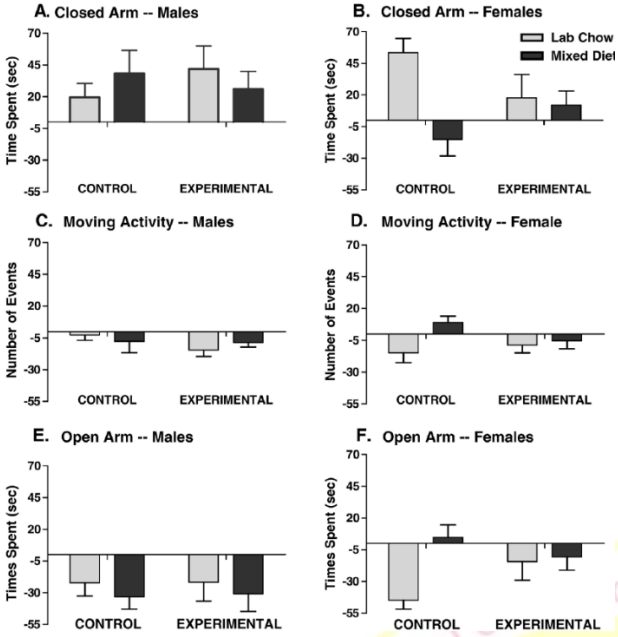

Figure 1. This figure shows the performance of rats in the elevated plus maze, including data on time spent in open and closed arms, number of entries, and mobility (Liang *et al.* 2008).

Advances and Critiques in Anxiety Behavioral Models

The EPM was validated by Pellow *et al.* (1985) as a sensitive assay for detecting anxiolytic and anxiogenic drug effects, confirming its construct and predictive validity for benzodiazepine-like compounds (Pellow *et al.* 1985). However, Fraser et al (2010) argued that the EPM and other models often lack sensitivity for newer pharmacological agents and are limited by their reliance on locomotor activity and novelty. Such concerns align with broader critiques advocating for diversified and refined behavioral paradigms that better capture the multifaceted nature of anxiety disorders (Fraser *et al.* 2010).

Hånell and Marklund (2014) highlighted the challenges of methodological variability, including strain differences and motor impairments, which undermine the translational validity of rodent behavioral tests used in drug discovery (Hånell and Marklund 2014). They stressed the importance of integrating behavioral data with neurobiological markers to enhance the robustness and relevance of these models. This aligns with calls by Ennaceur (2014) and File (2001) for multimodal approaches combining behavioral, physiological, and molecular data (Ennaceur 2014) (File 2001).

Benmhammed *et al.* 2019, underscored the influence of early-life experiences and environmental factors on anxiety phenotypes, highlighting the complexity of behavioral outcomes in animal models (Benmhammed *et al.* 2019). Calhoon and Tye (2015) further contributed by mapping neural circuits and genetic factors underpinning anxiety disorders, advocating for combining clinical and preclinical data to improve treatment strategies (Calhoon and Tye 2015).

Broader Implications and Methodological Recommendations

Behavioral toxicology, as discussed by Boyes (2007), benefits from standardized and rigorously controlled protocols to detect subtle neurotoxic effects before structural damage occurs (Boyes *et al.* 2007). Spanagel (2017) reviewed addiction models, emphasizing the influence of genetic and environmental variables on behavior and the necessity of integrating molecular analyses to improve translational relevance (Spanagel 2017). These perspectives echo across behavioral neuroscience, highlighting the complexity of interpreting rodent behaviors in the context of anxiety, emotionality, and stress (Lezak *et al.* 2017).

Advances in Neurophysiological Correlates of Heat Stress and Anxiety

Recent advancements in electrophysiological techniques have provided more detailed insights into the neural mechanisms underlying heat stress-induced behavioral changes. Studies using EEG and fMRI have shown that hyperthermia affects brain regions critical for emotional regulation, including the prefrontal cortex, amygdala, and hippocampus (Sun *et al.* 2013; Zhou *et al.* 2023). These changes correlate with heightened anxiety-like behaviors and impaired cognitive functions observed in animal models. Moreover, alterations in neurochemical signaling pathways, such as increased corticosterone release and altered neurotransmitter dynamics (e.g., glutamate and GABA balance), have been implicated in mediating the stress response to elevated temperatures (Mikasova *et al.* 2017). These findings suggest that integrating neurophysiological and behavioral data can provide a more comprehensive understanding of the multifaceted impact of thermal stress on brain function.

Integration of Behavioral and Molecular Approaches in Anxiety Research

The complexity of anxiety and emotionality in animal models has prompted researchers to move beyond purely behavioral assessments towards integrative approaches that combine molecular, genetic, and physiological data. For example, gene expression profiling of stress-related genes such as CRH (corticotropin-releasing hormone) and BDNF (brain-derived neurotrophic factor) in the hippocampus and amygdala have revealed distinct molecular signatures associated with anxiety-like behavior induced by heat stress (Chauhan *et al.* 2021; Ghasemzadeh *et al.* 2020). This integrative approach helps clarify the biological underpinnings of behavioral phenotypes and improves the translational relevance of animal studies by linking observable behaviors with neurobiological changes.

Role of Early-Life Stress and Environmental Factors in Shaping Anxiety Responses

Early-life environmental conditions have been shown to critically influence the development of anxiety-related behaviors and susceptibility to heat stress later in life. Prenatal and neonatal stress exposure can program the

hypothalamic-pituitary-adrenal (HPA) axis, resulting in altered stress responsivity in adulthood (Juruena *et al.* 2021). Animal studies have demonstrated that rodents exposed to early-life stress exhibit heightened anxiety-like behavior and exaggerated physiological responses when subjected to thermal stress, underscoring the interaction between developmental history and environmental challenges (He *et al.* 2020). Such findings highlight the importance of considering life-history factors when interpreting behavioral outcomes and designing intervention strategies.

Emerging Behavioral Paradigms and Technological Innovations

In addition to traditional tests like the open field and elevated plus maze, newer behavioral paradigms have been developed to provide more ethologically valid and nuanced assessments of anxiety and emotionality (Gencturk and Unal 2024). For instance, touchscreen-based cognitive testing and automated home-cage monitoring systems allow for continuous, less intrusive measurement of behavior under more naturalistic conditions (Pais *et al.* 2025). These methods reduce confounding influences such as novelty-induced stress and human handling, increasing reliability and reproducibility. Advances in machine learning and computer vision are also enhancing the ability to detect subtle behavioral phenotypes, enabling more precise classification of anxiety states and prediction of outcomes such as mortality risk under heat stress (Park *et al.* 2024). Incorporating these innovative technologies promises to overcome many limitations of conventional behavioral assays.

Overall, these studies collectively underscore the profound impact of environmental stressors like heat on animal behavior, the need for cautious interpretation of traditional behavioral assays, and the imperative for developing more refined, multimodal models to better understand the neurobiological basis of anxiety and stress-related disorders. (Table 1).

The authors characterise stress-induced hyperthermia as an acute response that occurs in the short term in individuals who are exposed to a stressful stimulus, and that this might reveal stress. They suggested that temperature stimulus, by producing energy resources used, increases the effects of cardiovascular (Mota-Rojas *et al.*2021). The brain's direct and indirect actions on the cytokines interleukin and tumor necrosis factor cause an increase in body temperature, serving as an endogenous pyrogen. At higher temperatures, cancerous or tumor cells can be damaged by hyperthermia, which is described and used to evaluate the effect of medications on learning and memory in rats and mice using transfer latency as a metric for memory acquisition and retention on an elevated plus maze ((Luheshi 1998; Sharma and Kulkarni, 1992).).

Table 1. Summary of behavioral changes observed in rats under thermal stress across different studies

Study	Temperature Condition	Behavioral Test Used	Observed Effects
Smith *et al.* , 2017	Heat (42°C for 4 h)	Open Field Test	↓ locomotion, ↑ anxiety
Chen *et al.* , 2018	Cold (4°C for 2 h)	Elevated Plus Maze	↓open arm time, ↑ freezing
Rao *et al.* , 2020	Heat stress (repeated)	Morris Water Maze	↓ memory retention, slower escape latency
Patel *et al.* , 2021	Cold exposure (acute)	Y-Maze	↓ spontaneous alternation, indicating cognitive decline
Kumar *et al.* , 2023	Heat (chronic exposure)	Open Field & Novel Object	↓ novelty interaction, ↑ thigmotaxis (anxiety-like signs)

Certain clinical ultrasound modalities have the potential to cause tissue heating (Figure 2).

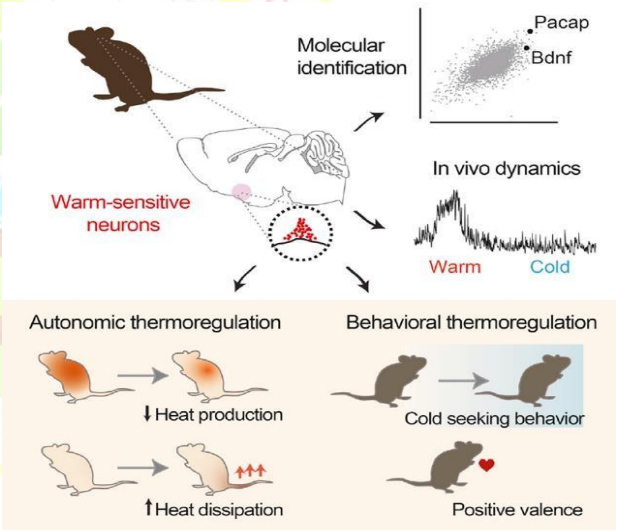

Figure 2. Warm-Sensitive nerve cells which Regulates the body temperature 2016

CONCLUSION

This review has summarized various studies investigating the behavioral and physiological responses of rats exposed to extreme environmental temperatures, including acute and chronic heat stress conditions. The findings suggest that high-temperature exposure leads to significant alterations in sleep patterns, body temperature, body weight, and electrophysiological parameters such as EEG and ECG. Behavioral assays, like the elevated plus maze, have consistently shown increased anxiety-like behaviors under thermal stress. These changes reflect the activation of stress response

pathways, particularly the hypothalamic-pituitary-adrenal (HPA) axis, and support the use of these biomarkers for evaluating thermal stress impacts. Understanding these effects is crucial for improving animal welfare in research settings and can inform biomedical research where hyperthermia is either a variable or a therapeutic tool. Future studies should integrate advanced techniques such as machine learning for more precise analysis and prediction of thermally induced behavioral outcomes.

AUTHORS CONTRIBUTIONS

All authors contributed to the study conception and design. The first draft of the manuscript was written by Anjali Kumari, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

CONFLICT OF INTEREST

The author here declares that there is no conflict of interest in the publication of this article.

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