New Approaches in Exercise Physiology (NAEP)
Vol. 6, No.11, June 2024
www.nass.atu.ac.ir
DOI: 10.22054/nass.2025.84633.1171

ATU PRESS

Innovative Approaches in Understanding the Stress Hyporesponsive Period: The Role of Exercise Physiologists in Unraveling its Unknown Mechanisms

Mahdi Shams –

Department of Exercise Physiology, Faculty of Sports Sciences, Allameh Tabataba'i University, Tehran, Iran.

Original Research

Received: March 01, 2024 Accepted: March 31, 2024

Abstract

Stress is a fundamental response of the body to various environmental pressures, impacting physical and mental health across age groups. After birth, infants enter a phase known as the Stress Hyporesponsive Period (SHRP), during which their physiological responses to stressors are significantly diminished. This stage is crucial as it shapes how individuals respond to stress later. Research indicates that the type and severity of stress experienced during the SHRP can have long-lasting implications, affecting stress reactivity in adulthood. Consequently, there is growing interest in utilizing exercise and physical activity as tools to mitigate the effects of stress. Various sports strategies and exercise regimens are adopted by health professionals to manage both physiological and psychological stressors. Notably, exercise has emerged as an important therapeutic option for various medical conditions, contributing to improvements in individuals' mental well-being and physical fitness. Moreover, the objectives of this research extend beyond mere treatment; they also involve the enhancement of individuals' physiological traits. This study examines the scientific literature over the past decade regarding the Stress Hyporesponsive Period

– Corresponding Author: shamsmahdi000@gmail.com
How to Cite: Shams, M. (2024). Innovative Approaches in Understanding the Stress Hyporesponsive Period: The Role of Exercise Physiologists in Unraveling its Unknown Mechanisms, *Journal of New Approaches in Exercise Physiology*, 5(10), 49-75.
DOI: 10.22054/nass.2025.84633.1171

and analyzes research articles. By focusing on the relationship between exercise and stress response, this research aims to fill existing gaps and explore new pathways for understanding the interactions between physical activity and stress responses.

Keywords: Stress Hyporesponsive period, Physical activity, Hypothalamic-pituitary-adrenal axis, Exercise

Introduction

the human body, from the very first day of life until the moment of death, constantly responds to various stress-inducing stimuli; any factor that disrupts the body's state of homeostasis is considered stress. In other words, any physical or biochemical factor that leads to a reaction in tissues and cells is a form of stress. However, this physiological response of the body is not the same under different conditions and ages, and, at the same time, the body responds to these stimuli with various mechanisms. In Taylor's study in the mid-1950s, it was reported that infants show significantly less response to stress compared to adults, and this led to the emergence of a new avenue of research (JAILER, 1950). The most important organ in response to stress is the brain, which alerts the organs to stress-inducing factors through hormonal and neurohormonal mechanisms. Hans Selye, a pioneer in the scientific understanding of stress, stated in his later years that stress is closely aligned with hormonal factors in the body. Selye's perspective was later analyzed more extensively; the human brain is a system sensitive to all internal and external events, activating response mechanisms with the help of specific peptides (Schmidt, 2019; Selye, 1955). The primary way the body responds to stress is through an axis formed by three hormone-secreting and neurohormonal glands. This common mechanism, known as the hypothalamic-pituitary-adrenal (HPA) axis, ultimately leads to the secretion of cortisol from the adrenal cortex, which is known as the stress hormone at high levels. The stress response in humans has been a survival factor throughout various periods of evolution. On the one hand, the body's response to stress is very complex and is not limited to a single pathway; the locus coeruleus and the parabrachial nucleus initiate the brain's response to stress-inducing stimuli through related yet separate mechanisms. The result of these two systems is the secretion of a group of hormones, including catecholamines and corticosteroids, from the superficial and deep parts of the adrenal glands, which play important roles in the stress response. Shortly after hypotheses regarding infants' lesser response to stress compared to adults were proposed, Taylor, using the measurement of

adrenal ascorbic acid changes—a suitable marker for measuring stress—asserted that infants exhibit no response to stress (JAILER, 1950; VanItallie, 2002). In 1960, Shapiro labeled this lack of response in infants to stress as the period of stress non-responsiveness, or SNRP. Later, with the advancement of radioimmunoassays that provided a more precise indication of brain responses, it became clear that the brain's response during this early phase of life does not reach zero, and the adrenal glands are still capable of secreting some corticosterone. It is believed that this low response to stress in infants is part of the developmental process of stress-related areas in the brain, which can shape individuals' behavior and responses to stress in adulthood (Selye, 1955). This indicates that this temporal window that opens during a specific period can lead to the development of lasting traits in individuals. These traits, which can influence an athlete's abilities, may be part of the factors examined in an athlete's success or failure in sports disciplines. Due to the stress-inducing nature of sports activities and events, as well as the impact of individual characteristics on purposeful physical activity, we aim to highlight the role of sports and the less explored research opportunities related to these concepts while reviewing studies in the area of stress non-responsiveness. Considering the lack of similar studies, the goal of this research is to increase awareness among exercise physiologists regarding SHRP to initiate future research.

Stress Hyporesponsive Period mechanisms

Examining the early life events is not only vital for understanding the neural and hormonal mechanisms during early life but also leads to a better understanding of individuals' responses in adulthood. To date, genetic traits and the type of training have generally been the factors studied in athletes; however, a group of characteristics in athletes may be inherited from periods over which the individual had no control, such as the postnatal period, during which the individual has no self-awareness but can significantly influence the unique traits of the athlete. In humans, various stresses from birth can lead to the emergence of

psychiatric disorders and other reactions. It can be said that the most significant influence an individual receives from their environment at birth is through their relationship with their mother. This period is crucial for shaping the physiological and neural pathways of the individual and also has a profound impact on the degree and manner of their response to stress in adulthood. Understanding how the nervous and endocrine systems are influenced by experiences at a young age can be very beneficial for establishing an appropriate pattern for addressing the various reactions of an individual, whether they are an athlete or a non-athlete (Murgatroyd et al., 2015). During the first week of life, wild rats of different breeds experience the highest levels of nursing and licking from their mothers. Similarly, in humans, the initial moments of newborns are spent in their mother's arms while breastfeeding, and the absence of this occurrence induces a type of anxiety and stress in infants. In rats, there is generally a period between 4 to 14 days during which they show the lowest hormonal response to stress; this period is known as the hyporesponsive period (Iwasa et al., 2012; Schmidt, 2019). Infants who experience specific stress during this low-response period may have their stress reactions affected later in life. Henriksen demonstrated that infants who received less maternal licking during childhood showed fewer estrogen and oxytocin receptors in the periventricular nucleus (PVN), medial preoptic area (MPOA), bed nucleus of the stria terminalis (BNST), lateral septum, and central amygdala. These areas play many roles in physiological functions and behaviors in the brain. This study showed that higher levels of maternal licking increase serotonergic activity in the hippocampus as well as plasma oxytocin levels; however, they do not prevent the increase of cortisol and corticosterone in response to cold stress in 13-day-old mice, which is contrary to reports regarding adult animals. The cumulative effect of maternal care increases the circulation of serotonin HT5 receptors in the hippocampus of infants with high licking compared to those with low licking. A previous study has shown that higher expression of glucocorticoid receptors in the hippocampus of infants may provide a more efficient negative feedback mechanism of the HPA

axis for offspring with high licking in adulthood (Champagne & Curley, 2009; Murgatroyd et al., 2015) (Figure 1). The HPA axis is not the only axis influenced by this period; it is assumed that exposure to stress during the Stress Hyporesponsive Period (SHRP) alters brain growth patterns to help cope with stressful environments (Munkhzaya et al., 2015; Shanks et al., 1995). Assuming that the factors regulating gonadotropin may reflect the hyporesponsive period to stress, a study in 2015 measured serum and hypothalamic luteinizing hormone concentrations, mRNA levels of gonadotropin-regulating factors, Kisspeptin receptor 1 (r1Kiss), and, for example, Kisspeptin (1Kiss) and gonadotropin-releasing hormone (GnRH) after intraperitoneal injection of lipopolysaccharide. Specifically, the serum concentration of luteinizing hormone in male and female rats was not affected by lipopolysaccharide injection until day 15 after birth, while it decreased after lipopolysaccharide injection on day 25 after birth. The levels of mRNA expression of the 1Kiss gene, r1Kiss, and GnRH in the hypothalamus did not differ at any time point between the lipopolysaccharide and control groups in both sexes. These findings suggest that gonadotropin-regulating factors indicate hyporesponsive periods to stress. The hypothalamic-pituitary-gonadal (HPG) axis may respond to immune stress between 15 and 25 days after birth, which could be associated with increased cytokine expression in the hypothalamus. A previous study by the same group showed that, in male rats, luteinizing hormone secretion was not affected by lipopolysaccharide injection on day 10 after birth, while it decreased with lipopolysaccharide injection on days 15 and 25 after birth Additionally, the immune system response, including inflammatory cytokines, can lead to disturbances in the hypothalamic-pituitary-gonadal (HPG) axis (Munkhzaya et al., 2015). These studies indicate that both the HPG and HPA axes can undergo significant changes and alterations in response to stress in SHRP. Physical activity can lead to various axis responses in the body; the reaction of these axes can undergo changes in the long term. Additionally, our understanding and behavioral responses to the nervous and hormonal reactions of these

axes can develop into a sort of physical memory in response to repeated exposure to stressors.

For example, a skydiver may exhibit different hormonal and nervous reactions after facing a stressful moment or jumping from a height compared to an inexperienced individual. This could result from physiological adaptation to stress and changes in the stress-responsive axes, or perhaps the individual has achieved resilience. This means that their understanding and behavior toward their hormonal and nervous responses to stress have become a sort of memory, and this repetition of stressors doesn't push the individual to react as intensely as others, despite similar hormonal and nervous responses.

Can we say that a soldier who has a higher fighting spirit, courage, avoidance of anxiety and fear, and risk-taking than their comrades has simply received more effective training, or are they genetically predisposed to this? We assume that these open time windows during specific life periods, such as infancy or puberty, regulate people's reactions in adulthood. However, the main question is whether this unconscious adjustment, beyond our control, can be re-regulated through a series of exercises and interventions or at least have its negative effects mitigated. This is where the role of exercise physiologists in this process, which has thus far been primarily studied in medical sciences, becomes clearer.

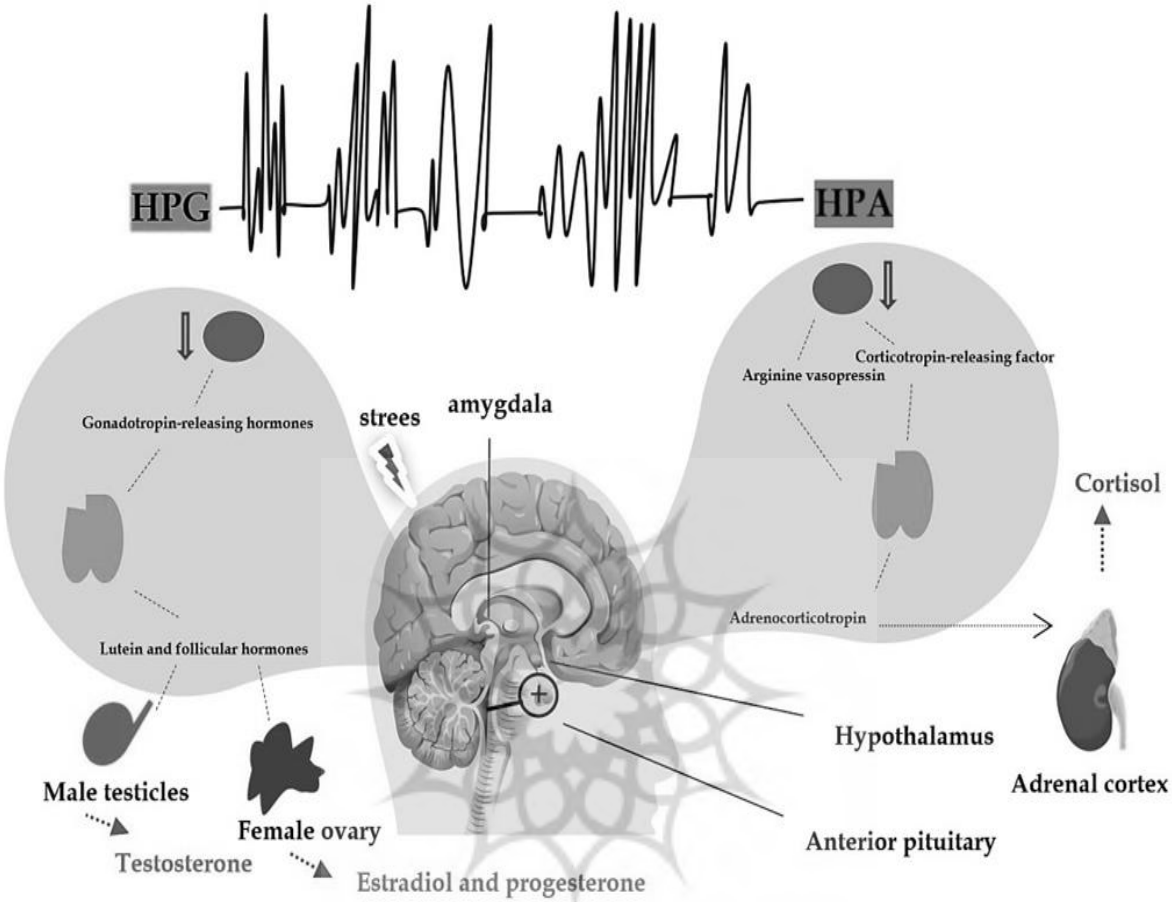

Figure 1. The hypothalamic-pituitary-adrenal (HPA) axis and the hypothalamic-pituitary-gonadal (HPG) axis are two important hormonal systems in the body. The HPA axis is activated by the secretion of corticotropin-releasing factors and arginine vasopressin from the hypothalamus, leading to the release of adrenocorticotropic hormone from the anterior pituitary, which in turn stimulates the secretion of cortisol from the adrenal cortex. In contrast, in the HPG axis, the secretion of gonadotropin-releasing hormones in the hypothalamus leads to the release of luteinizing and follicle-stimulating hormones from the anterior pituitary, resulting in the secretion of male and female sex hormones from the associated glands. These two axes are significantly influenced by stress experienced during the stress hyporesponsive period (SHRP) for adulthood.

Childhood Stress, Adult Response

Neural development occurs during the postnatal period; many studies have shown that there is a postnatal period during which individuals exhibit a diminished neural and hormonal response to stress. This critical period appears to allow different parts of the brain and neural axes to be regulated without an increase in cortisol, corticosterone (CORT), and pro-inflammatory mediators that can have detrimental effects on these pathways. Various factors can cause lasting changes in these neural and hormonal pathways in individuals. In 2017, Karen and colleagues conducted a study accepting the hypothesis that tactile stimulation (TS) minimizes fear, anxiety behaviors, and addiction to stimulant drugs in infants. They examined various postnatal periods of rodent pups with TS intervention at different times (Antoniazzi et al., 2017). As stated, SHRP has a biological function to protect the developing brain from fluctuations caused by circulating glucocorticoid stress (GC). After periods of increased corticosterone levels due to stress, suppression of brain-derived neurotrophic factor (BDNF) may occur. BDNF is a powerful growth factor that is expressed and released in the hippocampus, and it has been reported to significantly impact synaptogenesis and spine formation, neuronal survival, as well as neurogenesis in adult hippocampus (Lipsky & Marini, 2007; Yoshii & Constantine-Paton, 2010). Tactile stimulation (TS) in mice was designed by Karen to determine at what stage manipulation could enhance cognitive and motor growth and reduce symptoms similar to anxiety in the future. Overall, it was shown that if TS is applied between days 8 and 14 postnatal, it can modulate anxiety and improve memory parameters, which were not observed in other controlled groups. In fact, TS in the first week of life was associated with increased signs of anxiety and stress, while TS from postnatal day 15 (PND) to 21 resulted in a reduction. Additionally, TS in the second week of life led to a decrease in plasma corticosterone and hippocampal lipid peroxidation, an increase in catalase activity in the same brain region, and changes in BDNF and glucocorticoid receptor (GR) content in the hippocampus. TS across different postnatal periods was able to improve cognitive

behavior parameters related to exploratory behavior. The findings indicate that TS applied from PND 8 to 14 and from PND 15 to 21 was able to reduce plasma CORT levels, which highlighted the beneficial effect of this method on neuroendocrine function, especially in the second week of life, when this hormone is reduced. Considering the decrease in CORT levels and behavioral outcomes, it can be concluded that TS can reduce feelings, anxiety, and fear-like symptoms throughout adulthood by regulating HPA axis activity. The study by Borges Aguirre and colleagues in 2018 investigated whether stress experienced during SHRP affects fear and anxiety levels in adulthood (Borges-Aguiar et al., 2018). Following this hypothesis, the impact of maternal separation on newborn mice was analyzed in relation to fear levels in adulthood. There is substantial evidence indicating that the gray matter surrounding the periaqueductal gray (PAG) plays a critical role in panic disorder (PD) and panic attacks. Electrical stimulation of the dorsal PAG can evoke panic-like symptoms, which include severe anxiety, the urge to flee, shortness of breath, palpitations, chest pain, and feelings of suffocation, all of which occur without activation of the HPA axis. Recent data have generated unlikely cognitive theories that equate panic with anxiety. Ultimately, recent studies have shown that the PAG has a hypoxia-sensitive alarm system that is activated by hypercapnia and is inhibited by effective clinical treatments with panicolytic medications such as fluoxetine, clonazepam, and alprazolam (Clark, 1986; Müller et al., 2017; Schimitel et al., 2012). Separation from the mother during childhood is a type of stress imposed on the newborn, referred to as childhood separation anxiety (CSA). The present study showed that separation from the mother during the sensitive period increases the vulnerability of adult mice to panic and stress (Borges-Aguiar et al., 2018). Although the scientific literature on this subject shows contradictory results, Mishra and colleagues reached nearly similar findings to Borges Aguirre in a well-designed study conducted in the same year (Mishra et al., 2019). In this study, the effects of an auditory stimulus and an electric shock that induce fear were examined in mice that experienced maternal separation stress during the sensitive period

(SHRP) compared to a control group. A key feature of this study was the consideration of age as a variable in the type and level of response to the fear-inducing stimulus. The limbic circuit in infants can be influenced by cortisol levels during childhood. Studies have also shown that panic reactions, depression, anxiety, and hallucinations increase with an increase in adverse experiences in early childhood (Mishra et al., 2019). In addition to clinical evidence, studies also show that exposure to stress during the "critical time window" can lead to increased anxiety by enhancing fear memory retention in adult male Sprague-Dawley and Wistar rats (Kosten et al., 2006; Madruga et al., 2006; Sampath et al., 2014). Mishra's study showed that in adulthood, unlike the adolescent (5 weeks) and elderly (1 year) age groups, there is a profound effect on fear retention and memory extinction following stress from isolation or maternal separation. The increase in fear retention memory, along with a disruption in memory extinction, indicates that isolation stress during the sensitive period (SHRP) affects retention but not acquisition in the two distinct stages of fear conditioning—fear acquisition and fear extinction learning. This suggests that hormonal changes occurring during early youth (8 weeks) appear to play a significant role in disrupting memory retention. Dawn and colleagues used a maternal and social deprivation (MSD) model to investigate the effects of early life stress on neural stem cells (NSCs) and neurogenesis in adult brains; this study revealed that MSD during the stress hyporesponsive period (SHRP), when corticosterone release is suppressed, increases the NSC population size, whereas the same stress beyond the SHRP negates these effects. Early MSD increased neurogenesis not only in the dentate gyrus of the hippocampus, a classic neurogenic region, but also in the amygdala. Additionally, the results indicate that mice experiencing MSD stress during the SHRP show decreased amygdala/hippocampus-dependent fear memory. Sharma and colleagues also showed that stress experienced during the sensitive period (SHRP) affects the level of risk-taking behavior at different ages (Sharma et al., 2022). Uncontrolled risk-taking can harm the physical and mental health of individuals at various ages. A study conducted in

2023 assessed the risk-taking behavior of mice using a risky decision-making task (RDT). In this study, the mice were divided into two groups: the first group was exposed to isolation and maternal separation stress for 6 hours daily over a 10-day period during the stress hyporesponsive period (SHRP) from days 4 to 13 post-partum. These mice underwent RDT during adolescence. The second group, which experienced no stress during the SHRP, was chosen as the control group. The results indicated a decrease in risk delay and risk assessment in the maternal separation group, reflecting a greater tendency toward risk-taking behavior in these mice (Chowdhury et al., 2023). The latest study conducted in September 2024 by an Indian researcher was designed with a different pattern compared to other studies. This study examined the long-term effects of maternal separation stress in adulthood; however, unlike previous studies, which generally tested maternal separation stress between days 4 to 14 post-partum, this study sought to investigate the effects of late maternal separation (LMS) from days 10 to 21 post-partum in the tested mice. The results showed that male LMS mice were more resilient to anxiety induced by chronic variable stress (CVS) and exhibited less depressive-like behavior; in contrast, female LMS mice were equally resilient as non-LMS female mice. Additionally, increased expression of NPY , NPY1R, NPY2R, NPFFR1, and NPFFR2 was observed in the hypothalamus of male LMS mice, while these effects were reversed in the hippocampus. No changes in circulating corticosterone levels in response to psychological or physiological stressors were observed in either male or female groups (Ojha et al., 2024).

Studies show that the sensitive period (SHRP) is a critical phase in brain development that is susceptible to many interventions, and its changes can have lasting effects; this evidence makes further investigation of this time window essential.

Figure 2. The items reviewed in the most important articles listed in the last ten years. Evidence suggests that individuals' behavior and temperament traits can be influenced by various interventions received during the time window of SHRP.

Physical Activity and Stress

Hyporesponsive Period

Physical activity functions as a form of stress that compels the body to react. It can elicit responses in all bodily components, from the cellular level to tissues, organs, and various systems, such as the cardiovascular and respiratory systems. Furthermore, physical activity can simultaneously influence multiple physiological factors. Stress is a factor that disrupts homeostasis within the body; however, the imbalance caused by physical activity is manageable at acceptable levels and can place the body in a better condition post-recovery. This implies that we can categorize stress into two groups: positive-impact stress and negative-impact stress. For instance, stress arising from various diseases due to physical activity may enhance the body's condition.

The body's response to stress occurs at multiple levels, with the degree of reactivity being influenced by several factors, one of which is the body's stress reactivity. This reactivity is regulated within various temporal windows across different ages. The initial phase during which the body begins to regulate and develop the stress response system is known as the Stress Hyporesponsive Period (SHRP). During this period, the human body adjusts the primary mechanisms of the stress response through yet-to-be-identified mechanisms. This time window acts as a feedback system that programs age-related responses in accordance with the existing stress levels and surrounding environment. In other words, this period seems to determine how an individual should respond to stress.

As previously mentioned, the primary pathways for stress responses are the hormonal and neural regulatory axes, with the hypothalamic–pituitary–adrenal (HPA) axis being the most prominent, activated during stress. The ability of physical activity to stimulate this axis has been extensively studied for a long time. A study conducted in 2019 examined the effects of endurance and resistance training on the HPA

axis. This research indicated that the hypothalamic–pituitary–adrenal axis is stimulated by acute exercise, initiating multiple neuroendocrine cascades. Specifically, both corticoid levels and growth hormone concentrations are affected by homeostatic disruptions induced by exercise. The nature of these changes has been shown to depend on the type of exercise and the intensity and duration of the activity.

Recent findings (from the past 2–3 years) align with classical studies on the HPA axis, reporting that growth hormone concentrations typically increase during acute exercise—especially in high-intensity scenarios—while cortisol concentrations may either increase or decrease in response to acute exercise, consistent with the known intensity threshold effect. Future research should consider the synchronicity between these neuroendocrine cascades and other physiological systems (Anderson et al., 2019). Martin Douglas indicated in his study that exercise is a powerful physiological stimulus for the hypothalamic–pituitary–adrenal (HPA) axis. Two primary factors regulate the HPA axis response to exercise: intensity and duration. Endurance training does not automatically lead to chronic hypercortisolism, as trained endurance individuals exhibit similar biological markers of HPA axis activity at rest compared to healthy, untrained men. However, during HPA axis challenges, trained endurance athletes demonstrate an adaptive HPA axis response to repeated exercise, resulting from a reduction in tissue sensitivity to glucocorticoids. A considerable diversity of other mechanisms contributes to this adaptation, potentially acting at all levels of the signaling cascade and leading to the biological effects of corticosterone (Duclos, M et al., 2016). These studies demonstrate the responsiveness of the HPA axis to exercise-related stressors, with these effects potentially persisting in the long term. Additionally, numerous observations indicate that physical activity is associated with both reductions and increases in the activity of the hypothalamic–pituitary–gonadal (HPG) axis (Anderson et al., 2019). However, two notable points limit the generalizability of sports studies and the responses of

neuroendocrine axes to the Stress Hyporesponsive Period (SHRP). First, the SHRP represents a specific time window for the regulation of neuroendocrine axes that results in the development of a lasting trait in an individual; this state is a characteristic rather than a disorder or a continuous stressor. While various studies have explored how physical activity can activate neuroendocrine axes, such as the HPA axis, the ability of these axes to respond and change due to physical activity does not necessarily imply that such changes lead to a permanent reset or reconfiguration. Second, the SHRP occurs during infancy, limiting the potential for exercise interventions during this period, and no studies—whether in animal models or humans—have examined the effects of physical activity on stress responses through the lens of SHRP. Generally, physical activity improves the performance of various bodily systems; however, when we use the terms regulation and re-regulation, we imply our intent to implement changes toward our objectives, which can be either positive or negative. The primary goal of research in this area is, first and foremost, to identify and compare the physiological traits of individuals at different stages of SHRP to personalize interventions effectively. We believe that a significant portion of behavioral characteristics in sports is derived from neuroendocrine traits inherited from the SHRP and subsequent time windows, with genetic factors playing a lesser role.

Discussion

In the present study, we examined the literature from the last ten years on the stress hyporesponsive period. This period refers to the time window during the postnatal period when any intervention can have lasting effects. Behavioral traits of individuals, such as fear, anxiety, risk-taking, and various stress responses, may be shaped by this period, influencing the stress response mechanisms. This finding raises the question of how much living environment and the stressors imposed on the body affect reactions later in life. Several significant studies have been conducted in recent years in this area. A study published in 2018 titled 'Who Is Afraid of the Bad Big Wolf?' compared two groups of

wild deer living in different environments. The deer living in a lower-stress environment, where they faced less threat from predators, exhibited significantly lower cortisol levels, up to 30% less, compared to the higher-risk group (Bonnot et al., 2018). Animals can also adjust their responses to environmental changes they experience throughout their lives. For example, cues from predators may lead to the ontogenetic development of induced defenses in morphological structures and behaviors (Harvell, 1990). The ability to produce alternative phenotypes in response to environmental changes may allow organisms to maximize fitness by adapting their phenotype to prevailing environmental conditions. Human studies are less prominent due to the transformation of human life from a survival-based existence to a low-risk lifestyle today (Scheiner et al., 2019). Adaptability is a characteristic of all living organisms. Apart from genetic factors, the most important factor leading to differences between individuals is the type, intensity, and duration of the stressors that consciously and unconsciously affect a person from birth until death. Generally, two factors lead to one organism gaining an advantage over another: these are strengths and weaknesses. Improving strengths and controlling or reducing weaknesses depends on our understanding of where we have greater capacity for intervention and where intervention is less feasible or even impossible. This very characteristic of change and enhancement in humans allows an individual to excel in a sports event, gain superiority in a bloody battle, or even for one doctor to be better than another. The low-stress responsiveness period and the completion of brain development during infancy can be considered among those factors that can lead to the formation of strengths or weaknesses in a person during adolescence and adulthood.

The main limitation of this type of study is, first and foremost, that we cannot implement exercise interventions with infants. However, we can analyze human samples who have experienced various stressors and the effects of physical activity on them retrospectively. Additionally, similar to studies in the medical field, we can use animal samples with targeted athletic goals. Generally, animal studies in this area have

investigated the effects of stress interventions during the Stress Hyporesponsive Period on adult stress reactivity. Controlling this period in humans is challenging, and we cannot be certain about the types of stressors that infants experienced during that time. Animal studies help us understand how the factors regulated during the Stress Hyporesponsive Period, which manifest as traits and responses in adulthood, can be influenced by different types of physical activity. For instance, as mentioned in various studies, fear and anxiety behaviors are regulated during the Stress Hyporesponsive Period. The medical sciences approach has primarily focused on pharmacological research or identifying the causes of these issues in animal samples. However, traits such as fear, anxiety, and risk-taking are all aspects that become evident in sports and physical activity across various disciplines, especially in competitive or combative sports, and we need to seek alternative solutions beyond verbal methods for addressing these traits. Research indicates that until now, there has been no study examining and identifying the physiological characteristics of an athlete that may have been inherited from the stress hyporesponsive period. A sportsperson's superiority in a sporting event depends on various factors, including training, a suitable environment, genetic characteristics, and the stressors faced by an individual from birth or even during the fetal stage; the last point is the reason for this study. All these factors together lead to athletes participating in more events throughout their sports careers, achieving excellence, and experiencing a healthier retirement. One research potential in this area is examining the neurohormonal factors of individuals born in different neighborhoods and habitats and assessing their reactivity to the same stressors. Generally, children born in lower-resourced, more stressful environments tend to exhibit greater resilience and a stronger inclination to engage in higher-stress activities, such as combat sports, compared to those from more affluent neighborhoods. This suggests that, empirically, the living environment and environmental stressors can lead to the regulation of individuals' neurohormonal systems, which subsequently impacts their behavioral responses in adulthood.

Understanding the physiological markers of athletes in various disciplines, in relation to stressors that are beyond their control—such as those experienced during critical developmental windows—can be beneficial for understanding athletes' reactions and enhancing their performance. Exercise is a type of stress that activates the body's fight-or-flight systems, which triggers various axes of the hypothalamus-pituitary and activates sympathetic nerves. However, the stress from physical activity falls into the category of positive stress, which can have extensive effects on the body. The terms heterotopic and homotopic stress are classifications of stress first indirectly proposed by Hans Selye, the father of stress science, although the French surgeon Alexis Carrel was also among the first to contribute to the classification of stress. Homotopic stress refers to stress induced by similar stimuli affecting a specific tissue or cell type. This stress specifically impacts that type of tissue; when you engage in physical exercise, your muscles experience stress. This stress affects all muscle tissues, leading to their strengthening and growth. Alternatively, if you find yourself at a high altitude with less available oxygen, muscle tissues and cells respond similarly to this oxygen deficiency, creating mechanisms for survival and adaptation to the new conditions. On the other hand, heterotopic stress refers to a situation where stress in one tissue or type of cell is transferred to other tissues or cells with different characteristics. For example, inflammation; if an area of the body (like an inflamed joint) is under inflammatory stress, it may have negative effects on other organs such as the kidneys or liver. For instance, chronic inflammation can lead to changes in liver function. Additionally, psychological conditions like anxiety can physically impact the body, for example, by causing digestive problems or increasing blood pressure. Here, stress in the nervous system transfers to the digestive system, which has a different structure. These concepts demonstrate that the type of stress resulting from physical activity can be both homotopic and heterotopic. Any type of stress, whether positive or negative, takes the body out of homeostasis. But why do the outcomes of stressors not yield the same results? A group of studies has shown that physical activity can have

significant preventive and restorative properties for cognitive function and the brain (Lipsky & Marini, 2007). However, we believe that the scope of interventions to induce changes in brain levels and neural and hormonal axes is much greater than currently understood. Can we say that genetic characteristics and the type of training are the only factors that make a boxer more aggressive and combative than another, or what physiological factors influence a football player's risk-taking in the final moments of a match? One area that could be the subject of future studies is comparing the neurohormonal factors of athletes across different disciplines. For instance, examining and comparing levels of anxiety and fear in athletes from two different sports, yet with similar anthropometric and performance characteristics, in response to a specific stressor could provide deeper insights into how various training attributes influence behavioral reactions related to neurohormonal axes, such as the HPA axis. The strees hyporesponsive period (SHRP) could also be a new research avenue in sports sciences, as understanding the type and timing of intervention could address many of the limitations faced by athletes, particularly performance athletes. Additionally, since exercise now has a therapeutic approach, it can contribute to the recovery of individuals who have faced various stressors during this period. It seems that physical activity is the only means that allows us to reconfigure the pathways and axes that are only regulated during a specific timeframe in infancy. Based on this principle, extensive studies have focused on using sports interventions to treat many psychological disorders, including depression and anxiety, which are generally believed to have their roots in childhood (Gupta et al., 2024). Many studies have also shown that stressors experienced during the SHRP time window can be associated with individuals' responses to fear, anxiety, and risk-taking in adulthood. Although it may seem impossible to implement interventions during this time period, increasing our understanding of the events of this period in athletes can be crucial in recognizing the physiological characteristics of athletes and finding the appropriate range of interventions. Understanding the acquired and genetic physiological traits, in addition to talent identification in various

sports, can influence the selection of a player's position, the fighting style of a martial artist, or even the risk-taking and decision-making speed of a Formula One driver. We believe that among the strategies for managing stress, anxiety, fear, and controlling risk-taking in athletes—especially in high-stress and contact sports like martial arts—we should not limit ourselves to mental techniques and skills. Understanding the cellular mechanisms involved in each sport and determining the genetic profiles of individuals for appropriate interventions is essential. Prolonged exposure to stress can lead to an increase in hormones like cortisol, which can negatively impact learning, memory, and mental health. Some studies have shown that chronic stress can change the structure of the brain. Additionally, living in dangerous conditions may lead to an increase in fight-or-flight responses, which could enhance physical and mental capabilities in critical situations.

Conclusion

Generally, to improve conditions and help athletes manage stress and pressure, mental training and psychological techniques are utilized, or competitive simulations and training under pressure (such as friendly matches or training in challenging conditions) are used to normalize stressful situations. Although these processes can be very helpful, we believe they are not the only solutions available to us, and there is a sense of a gap in studies that track the stress-inducing factors in athletes at a cellular and mechanistic level.

Conflict of Interests

The authors declare that they have no conflict of interests to disclose.

Funding/Support

None.

ORCID

Mahdi Shams https://orcid.org/

Reference

Antoniazzi, C. T. D., Metz, V. G., Roversi, K., Freitas, D. L., Vey, L. T., Dias, V. T., Segat, H. J., Duarte, M. M. M. F., & Burger, M. E. (2017). Tactile stimulation during different developmental periods modifies hippocampal BDNF and GR, affecting memory and behavior in adult rats. Hippocampus, 27(2), 210–220. https://doi.org/10.1002/HIPO.22686

Anderson, T., Berry, N. T., & Wideman, L. (2019). Exercise and the hypothalamic–pituitary–adrenal axis: a special focus on acute cortisol and growth hormone responses. Current Opinion in Endocrine and Metabolic Research, 9, 74–77. https://doi.org/10.1016/J.COEMR.2019.08.002

Bonnot, N. C., Bergvall, U. A., Jarnemo, A., & Kjellander, P. (2018). Who's afraid of the big bad wolf? Variation in the stress response among personalities and populations in a large wild herbivore. Oecologia, 188(1), 85. https://doi.org/10.1007/S00442-018-4174-7

Borges-Aguiar, A. C., Schauffer, L. Z., de Kloet, E. R., & Schenberg, L. C. (2018). Daily maternal separations during stress hyporesponsive period decrease the thresholds of panic-like behaviors to electrical stimulation of the dorsal periaqueductal gray of the adult rat. Behavioural Brain Research, 344, 132–144. https://doi.org/10.1016/J.BBR.2018.02.020

Champagne, F. A., & Curley, J. P. (2009). Epigenetic mechanisms mediating the long-term effects of maternal care on development. Neuroscience and Biobehavioral Reviews, 33(4), 593–600. https://doi.org/10.1016/J.NEUBIOREV.2007.10.009

Cano Sokoloff, N., Misra, M., & Ackerman, K. E. (2016). Exercise, Training, and the Hypothalamic-Pituitary-Gonadal Axis in Men and Women. Frontiers of hormone research, 47, 27–43. https://doi.org/10.1159/000445154

Chowdhury, A., Sharma, S. S., Arjun, B. S., Pandya, H. J., Shankaranarayana Rao, B. S., & Laxmi, T. R. (2023). Risky decision-taking task: A novel paradigm to assess the risk-taking

behaviour in rats predisposed to early-life stress. Journal of Neuroscience Methods, 392. https://doi.org/10.1016/J.JNEUMETH.2023.109864

Clark, D. M. (1986). A cognitive approach to panic. Behaviour Research and Therapy, 24(4), 461–470. https://doi.org/10.1016/0005-7967(86)90011-2

Daun, K. A., Fuchigami, T., Koyama, N., Maruta, N., Ikenaka, K., & Hitoshi, S. (2020). Early Maternal and Social Deprivation Expands Neural Stem Cell Population Size and Reduces Hippocampus/Amygdala-Dependent Fear Memory. Frontiers in Neuroscience, 14. https://doi.org/10.3389/FNINS.2020.00022

Duclos, M., & Tabarin, A. (2016). Exercise and the Hypothalamo-Pituitary-Adrenal Axis. Frontiers of hormone research, 47, 12–26. https://doi.org/10.1159/000445149

Gupta, S., Bharatha, A., Cohall, D., Rahman, S., Haque, M., & Azim Majumder, M. A. (2024). Aerobic Exercise and Endocannabinoids: A Narrative Review of Stress Regulation and Brain Reward Systems. Cureus, 16(3). https://doi.org/10.7759/CUREUS.55468

Harvell, C. D. (1990). The ecology and evolution of inducible defenses. The Quarterly Review of Biology, 65(3), 323–340. https://doi.org/10.1086/416841

Iwasa, T., Matsuzaki, T., Murakami, M., Kinouchi, R., Gereltsetseg, G., Nakazawa, H., Yamamoto, S., Kuwahara, A., Yasui, T., & Irahara, M. (2012). Effects of lipopolysaccharide exposure at different postnatal time points on the response of LH to homotypic stress in adulthood. Journal of Reproductive Immunology, 94(2), 155–160. https://doi.org/10.1016/J.JRI.2012.02.003

JAILER, J. W. (1950). The maturation of the pituitary-adrenal axis in the newborn rat. Endocrinology, 46(5), 420–425. https://doi.org/10.1210/ENDO-46-5-420

Kosten, T. A., Lee, H. J., & Kim, J. J. (2006). Early life stress impairs fear conditioning in adult male and female rats. Brain Research,

1087(1), 142–150. https://doi.org/10.1016/J.BRAINRES.2006.03.009

Lipsky, R. H., & Marini, A. M. (2007). Brain-derived neurotrophic factor in neuronal survival and behavior-related plasticity. Annals of the New York Academy of Sciences, 1122, 130–143. https://doi.org/10.1196/ANNALS.1403.009

Madruga, C., Xavier, L. L., Achaval, M., Sanvitto, G. L., & Lucion, A. B. (2006). Early handling, but not maternal separation, decreases emotional responses in two paradigms of fear without changes in mesolimbic dopamine. Behavioural Brain Research, 166(2), 241–246. https://doi.org/10.1016/J.BBR.2005.08.005

Mishra, P. K., Kutty, B. M., & Laxmi, T. R. (2019). The impact of maternal separation and isolation stress during stress hyporesponsive period on fear retention and extinction recall memory from 5-week- to 1-year-old rats. Experimental Brain Research, 237(1), 181–190. https://doi.org/10.1007/S00221-018-5411-3

Müller, C. J. T., Quintino-dos-Santos, J. W., Schimitel, F. G., Tufik, S., Beijamini, V., Canteras, N. S., & Schenberg, L. C. (2017). On the verge of a respiratory-type panic attack: Selective activations of rostrolateral and caudoventrolateral periaqueductal gray matter following short-lasting escape to a low dose of potassium cyanide. Neuroscience, 348, 228–240. https://doi.org/10.1016/J.NEUROSCIENCE.2017.02.022

Munkhzaya, M., Matsuzaki, T., Iwasa, T., Tungalagsuvd, A., Kawami, T., Kato, T., Kuwahara, A., & Irahara, M. (2015). The suppressive effect of immune stress on LH secretion is absent in the early neonatal period in rats. International Journal of Developmental Neuroscience, 46(1), 38–43. https://doi.org/10.1016/J.IJDEVNEU.2015.06.007

Murgatroyd, C. A., Peña, C. J., Podda, G., Nestler, E. J., & Nephew, B. C. (2015). Early life social stress induced changes in depression and anxiety associated neural pathways which are

correlated with impaired maternal care. Neuropeptides, 52, 103. https://doi.org/10.1016/J.NPEP.2015.05.002

Ojha, R. K., Dongre, S., Singh, P., & Srivastava, R. K. (2024). Late maternal separation provides resilience to chronic variable stress-induced anxiety- and depressive-like behaviours in male but not female mice. The World Journal of Biological Psychiatry : The Official Journal of the World Federation of Societies of Biological Psychiatry, 25(7), 393–407. https://doi.org/10.1080/15622975.2024.2390411

Sampath, D., Sabitha, K. R., Hegde, P., Jayakrishnan, H. R., Kutty, B. M., Chattarji, S., Rangarajan, G., & Laxmi, T. R. (2014). A study on fear memory retrieval and REM sleep in maternal separation and isolation stressed rats. Behavioural Brain Research, 273, 144–154. https://doi.org/10.1016/J.BBR.2014.07.034

Schimitel, F. G., de Almeida, G. M., Pitol, D. N., Armini, R. S., Tufik, S., & Schenberg, L. C. (2012). Evidence of a suffocation alarm system within the periaqueductal gray matter of the rat. Neuroscience, 200, 59–73. https://doi.org/10.1016/J.NEUROSCIENCE.2011.10.032

Schmidt, M. V. (2019). Stress-Hyporesponsive Period. Stress: Physiology, Biochemistry, and Pathology Handbook of Stress Series, Volume 3, 49–56. https://doi.org/10.1016/B978-0-12-813146-6.00004-7

Selye, H. (1955). Stress and disease. Science (New York, N.Y.), 122(3171), 625–631. https://doi.org/10.1126/SCIENCE.122.3171.625

Scheiner, S. M., Barfield, M., & Holt, R. D. (2019). The genetics of phenotypic plasticity. XVII. Response to climate change. Evolutionary Applications, 13(2), 388. https://doi.org/10.1111/EVA.12876

Sharma, S. S., Srinivas Bharath, M. M., Doreswamy, Y., & Laxmi, T. R. (2022). Effects of early life stress during stress hyporesponsive period (SHRP) on anxiety and curiosity in adolescent rats.

Experimental Brain Research, 240(4), 1127–1138. https://doi.org/10.1007/S00221-022-06319-5

Sharma, S. S., Srinivas Bharath, M. M., Doreswamy, Y., & Laxmi, T. R. (2022). Effects of early life stress during stress hyporesponsive period (SHRP) on anxiety and curiosity in adolescent rats. Experimental Brain Research, 240(4), 1127–1138. https://doi.org/10.1007/S00221-022-06319-5

Shanks, N., Larocque, S., & Meaney, M. J. (1995). Neonatal endotoxin exposure alters the development of the hypothalamic-pituitary-adrenal axis: early illness and later responsivity to stress. The Journal of Neuroscience: The Official Journal of the Society for Neuroscience, 15(1 Pt 1), 376–384. https://doi.org/10.1523/JNEUROSCI.15-01-00376.1995

VanItallie, T. B. (2002). Foreword. Metabolism, 51(6), 1. https://doi.org/10.1053/META.2002.33182

Yoshii, A., & Constantine-Paton, M. (2010). Postsynaptic BDNF-TrkB signaling in synapse maturation, plasticity, and disease. Developmental Neurobiology, 70(5), 304–322. https://doi.org/10.1002/DNEU.20765

Corresponding Author: shamsmahdi000@gmail.com
How to Cite: Shams, M. (2024). Innovative Approaches in Understanding the Stress Hyporesponsive Period: The Role of Exercise Physiologists in Unraveling its Unknown Mechanisms, Journal of New Approaches in Exercise Physiology, 5(10), 49-75.
DOI: 10.22054/nass.2025.84633.1171.