

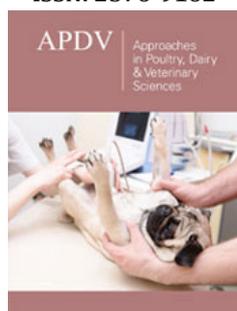
The Role of Major Hormones in Metabolic Adaptation of Farm Animals

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ISSN: 2576-9162



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Submission:  April 27, 2019

Published:  May 13, 2019

Volume 6 - Issue 1

How to cite this article: Dawit A, Tewodros A. The Role of Major Hormones in Metabolic Adaptation of Farm Animals. *Appro Poultry Dairy & Vet Sci* 6(1). APDV.000629.2019.
DOI: [10.31031/APDV.2019.06.000629](https://doi.org/10.31031/APDV.2019.06.000629)

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Abstract

Animals possess various inherent mechanisms to cope up with the changing environmental conditions. It has been observed that the ability of animals to adjust with these climatic extremes is related to their level of adaptation and this is inversely correlated with their production potential. Stress tolerance in livestock is determined through various mechanisms and metabolic neuroendocrine regulation is one of the crucial pathways by which the animal survives the stressful condition. The Hypothalamic-Pituitary-Adrenal (HPA) axis plays a significant role in the release of several neurotransmitters and hormones which regulates the thermoregulatory mechanisms in animals. The Thyrotropin-Releasing Hormone (TRH), Thyroid Stimulating Hormone (TSH) and Thyroid Hormones (T3 and T4) are the components of metabolic pathway in regulating body heat production. Thyroid hormones are recognized as the key regulators of metabolic activity in domestic animals. Further, leptin secreted from adipocytes also has a great influence in regulating whole body energy metabolism and may be attributed as a "metabolism modifier". The release of cortisol stimulates physiological and metabolic responses necessary to optimize the animal capacity to overcome a stressful factor by increasing the energy availability by decrease of cortisol levels. Generally, thyroid hormones, cortisol and leptin are considered to be important biological markers of neuroendocrine pathways for the regulation of metabolic adaptation mechanisms during stress in livestock.

Keywords: Livestock; Stress; Adaptation; Neuro-endocrine; Thyroid hormones; Cortisol; Leptin

Introduction

Climate change has emerged as the major threat to the world economy. It has turned up to be the global phenomenon threatening the survival of many ecosystems worldwide. The increased concentration of Greenhouse Gases (GHGs) in the atmosphere causes the greenhouse effect, resulting in climate change. Heat waves will occur more habitually and last longer that leads to extreme precipitation and fluctuating weather conditions in many regions of the world [1]. Increased frequency of life-threatening events like cyclones, droughts, floods, tsunami, and wildfires are expected to happen in the changing climate scenario. Among the agricultural sector, crops and livestock are particularly vulnerable to the devastating effects of climate change ultimately deteriorating the agricultural production [2]. A stressor is a chemical or biological agent, environmental condition, external stimulus or an event that causes stress to an organism and an event that triggers the stress response. Temperature is one of the most important influences on the immune system of animals and Procedural stressors are handling, shipping and disease treatments [3].

Livestock possess a wide range of adaptive mechanisms to cope with environmental challenges. Endocrine responses are one of the principal regulators of animal adaptation to heat and cold stress challenges. The Hypothalamo-Pituitary Adrenal (HPA) axis plays an integral role in regulating the neuroendocrine mechanism during stress condition [4]. Metabolic adaptation describes a macro-physiological pattern whereby respiratory estimates of metabolic rates of ectotherms from cold environments, typically from high latitudes or altitudes, tend to be elevated relative to those from warm environments [5]. This review is an attempt to gather information pertaining to neuro-endocrine mechanisms which help the livestock to survive in a specific environment also attempts to elucidate the mechanisms by which the production pathways are compromised in an effort to supply energy resources for maintaining the vital functions of the body

Major Hormones in Metabolic Adaptation

Effects of stress

Metabolic changes: High ambient temperature can adversely affect the structure and physiology of cells causing impaired transcription, RNA processing, translation, oxidative metabolism, membrane structure and function [6]. Cells generate small amounts of free radicals or Reactive Oxygen Species (ROS) during their normal metabolism. Although low levels of ROS are essential in many biochemical processes, accumulation of ROS may damage biological macromolecules i.e. lipids, proteins, carbohydrates and DNA [7].

Therefore, heat stress increased lipid per oxidation which was associated with production of large number of free radicals which are capable of initiating per oxidation of polyunsaturated fatty acids. Renaudeau D et al. [8] also reported that lipid per oxidation is significantly increased during reticulo-ruminal impaction in animals. Heat stress may lead to increased production of Transition Metal Ions (TMI), which can make electron donations to oxygen forming superoxide or H_2O_2 which is further reduced to an extremely reactive OH radical causing oxidative stress. Antioxidants, both enzymatic (viz. superoxide dismutase, glutathione peroxidase & catalase) and non enzymatic (Vitamins C, E and A, glutathione, pyruvate, etc.) provide necessary defense against oxidative stress generated due to high ambient temperature.

Feed intake and rumination: The negative effect of stress on feed intake has long been recognized, although the precise pathways involved are still debated. It is likely, however, that the inhibitory effect of stress on appetite results from a complex interplay among leptin, glucocorticoid and the CRF. There is some evidence suggesting that stress may have an inhibitory effect on rumination and this in turn may reduce feed digestibility and therefore performance and may also increase the risk of ruminal acidosis. The precise mechanism underlying the effect of stress on rumination is not known, but it is interesting to highlight that brain activity during rumination is similar to that during sleep, and stress is known to interfere with sleep. Animals exposed for nutritional stress would result depressed appetite, altered body fat ratio, weight loss, nutrient deficiency and eating disorders. Heat stress has long been known to adversely affect rumen health. Furthermore, due to reduced feed intake, heat-stressed cows ruminate less and therefore generate less saliva. The reductions in the amount of saliva produced and salivary HCO_3 content and the decreased amount of saliva entering the rumen make the heat stressed cow much more susceptible to sub clinical and acute rumen acidosis [9]. When cows begin to accumulate heat, there is a redistribution of blood to the extremities in an attempt to dissipate internal energy. As a consequence, there is reduced blood flow to the gastrointestinal track and nutrient uptake may be compromised [10].

Hormonal changes: It has been recognized that certain environmental stressors have the potential to activate the Hypothalamus Pituitary-Adrenal Cortical Axis (HPA) and sympatho-

adrenal medullary axis. There is increase in plasma concentration of Cortisol and corticosterone and less frequently an increase in plasma epinephrine and nor epinephrine concentration in heat stressed animals [11]. Sparke et al. [12] reported an increase in plasma prolactin concentration during thermal stress in dairy cows. Alteration in prolactin secretion may be associated with altered metabolic state of heat stressed animals. One possibility is that prolactin is involved in meeting increased water and electrolyte frequently demands of heat stressed animals.

Metabolic Adaptation of Farm Animals

Sparke et al. [12] defined adaptation as a modification in the animal's behavior or metabolic responses resulting from an experience that improves the ability of animal to cope with subsequent challenges. Prayaga KC & Henshall JM [13] also defined it as the ability to survive and reproduce within a defined environment. Barker JSF [14] defined adapted ness as the state of being adapted, the ability of breeds to produce and reproduce in a given set of environments, or the choice of particular breeds for specific environments. Adaptability is then a measure of potential or actual capacity to adapt in different environments [15]. Adaptation traits are usually characterized by low heritability. In relatively stable environments, such traits have probably reached a selection limit; however, they are expected to respond to selection if the environment shifts, thus resulting in changing fitness profiles and increases in heterozygosity [16].

Empirical evidence strongly supports the expectation that the genetic basis of population differentiation for fitness traits will be non-additive, with different adaptive gene complexes evolved in each breed.

Metabolic and hormonal acclimation to hot environment

Evidence suggests that within domesticated ruminants, differences exist between species, breed and production level with regard to heat stress susceptibility [17]. This is mainly due to species differences in the ability to reduce metabolic and endogenous heat production and increase heat dissipation. For instance, animals adapted to hot environments have lower metabolic and water turnover rates, and a higher capacity to dissipate heat via panting and sweating [18]. The lower basal heat production, larger salivary glands and thus saliva secretion, higher surface area of absorptive mucosa, increased efficiency in the ability to recycle urea from blood to the rumen (compared to other grass and roughage eaters) and a capacity to substantially increase the volume of the foregut when fed high fibrous feed are the main morpho-physiological characteristics that allow animals to more easily adapt to harsh environments. The increased susceptibility of cattle to heat stress is primarily due to their high metabolic rate, compared with that of other ruminants, and the poorly developed water retention mechanism in the kidney and gut [19].

In addition, beef cattle are less sensitive than dairy cattle to heat stress due to the overall decrease in endogenous heat production.

The level of acclimation to heat stress also varies among breeds within the same species and this is probably because *Bos indicus* and *Bos taurus* cattle have evolved within distinct climates. Acclimation responses also depend on pre-stress production levels. For example, low-yielding lactating cows are able to return to pre-heat stress production levels, but high producing cows cannot, and this may be because the zone of thermal neutrality shifts to lower temperatures, as milk yield, feed intake and metabolic heat production increase.

Neuro-Endocrine Adaptation

Hypothalamic-pituitary-thyroid axis

The Hypothalamic-Pituitary-Thyroid Axis (HPT) axis plays a critical role in the regulation of energy expenditure by affecting basal metabolic rate through the actions of thyroid hormones. The HPT axis is under the control of neurons located in the medial region of the PVN nucleus of the hypothalamus that synthesizes and release Thyrotropin-Releasing Hormone (TRH) into the pituitary gland [20]. The TRH stimulates the release of Thyrotropin (TSH) from the anterior pituitary, which in turn stimulate the synthesis and release of thyroid hormones in the target thyroid gland. Mainly two types of thyroid hormones are produced such as Tri-iodothyronine (T3) and Thyroxine (T4). The T3 is the main biologically active hormone recognized by its greater affinity for thyroid hormone receptors while T4 is the storage hormone which is converted to T3 by the activity of deiodinase enzymes located within most target tissues aided by the central nervous system [21].

Thyroid Hormones, Thyroxine (T4), and Triiodothyronine (T3) play an important role in the control of metabolic rate and thermogenesis and thus, in the ability of animals to maintain body temperature [22]. Specifically, these hormones increase thermogenesis by stimulating energy-wasting mechanisms such as the uncoupling of oxidative phosphorylation in the mitochondria [23], increase in ATP intake for the maintenance of transmembrane ion gradients (Na⁺ and K⁺ gradients across the cell membrane), and acceleration of metabolite turnover to maintain the metabolite concentrations constant (lipolysis and lipogenesis, glycolysis and gluconeogenesis cycles) [24]. In broad terms, thyroid hormones increase metabolism and, as a result, metabolic heat production. Therefore, heat acclimation comprises reduced thyroid activity and low circulating levels of T4 and T3 [25]. The activation of the Hypothalamic-Pituitary-Adrenal (HPA) axis and the consequent increase in circulating concentrations of cortisol is one of the most common response and non-specific response of an animal to stressful conditions [26].

Thyroid Hormones are recognized as the key regulators of metabolic activity in domestic animals [27]. Both acute and chronic stress causes transient activation of the HPT axis. This was facilitated by the increases in TSH concentration as a result of the direct stimulatory effect of glucocorticoids on the pituitary thyrotrope [28]. However, prolonged stress is invariably associated with decreased HPT activity in farm animals to reduce the

metabolic heat production during heat stress. Similarly, reduced HPT activity is mediated by glucocorticoids on TRH production in the Hypothalamus [29]. Likewise, increased somatostatin secretion as a result of enhanced intra-hypothalamic CRH release might also influence the reduced TSH secretion during heat stress [30]. In addition to the inhibition in TSH production, the extended activity of the HPA axis also reduces the conversion of T4 to T3 in peripheral tissues [31].

Leptin (Greek: leptos=thin) is a 16KDa peptide hormone and is generally produced in white adipose tissue. Its function is to signal the nervous system about the overall fat reserves of the body. It seems that leptin has a great influence in regulating whole body energy metabolism and may be attributed as a "Metabolism modifier". It is also accepted to be a biological marker that reflects the degree of fatness in the body. Leptin is encoded by LEP/Ob gene, comprises of three exons and two introns and is located on 4th and 5th chromosome in cattle [32] and sheep, respectively. Leptin has a role in regulating the energy balance when acts on nervous system (CNS) and affects deposition of fat in animals by controlling appetite and energy consumption. Leptin, through its receptors in the peripheral tissues, has been involved in several roles, including lipid oxidation, glucose metabolism, endocrine system, angiogenesis, blood pressure, cell differentiation & proliferation, brain development and wound healing [33].

The release of cortisol stimulates physiological and metabolic responses necessary to optimize the animal capacity to overcome a stressful factor by increasing the energy availability [34]. From these results, it appears that, while acute heat exposure leads to HPA axis stimulation as a result of the animal non-specific response to a stressful condition, heat acclimation most likely results in a decrease of cortisol levels. However, more investigations are needed in this pathway for understanding the underlying mechanisms pertaining to HPT axis in the future.

Significance of Livestock Adaptation

Even though climate change is a global phenomenon, its ill effects are experienced mostly by the poor people in developing countries due to their heavy dependence on the natural resources. The extensive housing system practiced in the country makes the animal more vulnerable to the climate change and the heat stress in particular [35]. The increased temperature during summer season has caused a significant barrier to livestock production by decreasing both the water and feed availability [36,37]. Therefore, to maintain the constant productivity in the changing climate scenario, the animal should be well adapted to the extreme conditions. Adaptability of an animal can be defined as the ability of an animal to survive and reproduce within a defined environment [38,39].

When the cows are exposed to a higher temperature than Thermal Neutral Zone (TNZ), they show various responses such as increased respiration rate, increased rectal temperature, decreased pulse rate, panting and profuse sweating and reduced feed

consumption. Reduction in the feed intake results in less available energy in the animal body during heat stress [40]. Utilization of this energy for the adaptive mechanisms further reduces the growth and development of the animal. But, according to [41], the energy produced through feed intake is not used for adaptive mechanisms; instead, the animal has the inherent capability to release energy from the alternate sources, which include the production of the glucose from lipid and protein. In such adapted animals, the energy produced through digestion is exclusively used for the growth and production. In most of the cases, livestock adapts to increased temperature and this is aided by the availability of other factors like feed and water. But in extremely hot conditions when food and water are not available their survivability will be questioned which may further lead to death if the extreme condition persists relatively for a longer period [42].

The vulnerability of the animal to the stress depends on the magnitude of the load to which the animal is exposed and the inherent genetic potential of the animal to cope up with the temperature [43]. It has been observed that the indigenous low producing cows are more adaptable to heat stress than the high producing exotic ones [44]. According to [45], beef cattle having strictly regulated body temperature showed greater productivity than those having varying body temperature. Under high heat loads, *Bos indicus* breeds and their cross breeds showed greater thermoregulation mechanisms through differences in metabolic rate, food and water consumption, sweating rate, coat characteristics and color compared to *Bos taurus* breeds [46].

Similarly, less water loss in desert sheep breeds than the arid and humid region shows its better adaptability to the heat stress [47]. Heat stress also affects the quality and quantity of production in poultry [48]. Thus, to improve or sustain production in the changing climate scenario the animal must be well adapted to the heat stress. The well-adapted animals require less energy to cope up with the temperature increase. In addition, increased feed conversion rate was also reported in adapted animals compared to the less adapted ones leading to increased profitability in rearing the adapted breeds in the fluctuating environmental conditions.

Conclusion

Stress has emerged as the major threat to the livestock production. Extended exposure of stress compromises the ability of farm animal to control the stress which ultimately affects their feed intake, milk production, and reproductive efficiency, also Stressors have additive effects include changes in the immune function and increased susceptibility to disease, resulting in severe economic constraints for farmers. Neuroendocrine response is the principal regulator of stress response in animals and it forms the basis for regulating and coordinating all other adaptive response in domestic animals. The Hypothalamic-Pituitary-Thyroid (HPT) axis plays a critical role in the regulation of energy expenditure by affecting basal metabolic rate through the actions of thyroid hormones. Thyroid hormones are recognized as the key regulators of metabolic activity in domestic animals. Therefore, understanding

in depth the various adaptive responses of animals may provide future directions for coping them to the devastating effects of stress.

Acknowledgement

Author's deepest gratitude goes to members of Department of Animal Sciences, College of Agriculture and Natural Resources Science, and the communities of Debre Berhan University.

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