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Opinion Paper

Climate change and hypothalamic–pituitary–adrenal axis in livestock: what we know and what needs to be explored?

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BACKGROUND

Climate change causes unprecedented challenge to the entire development of livestock production system. Climate change will negatively impact the animal directly through elevated temperature and precipitation pattern variation and indirectly through the reduced quality and quantity of crop yield, water availability and increased disease outbreaks. Among the all climatic variables, heat stress is the most intriguing factor which affects livestock sector. Heat stress detrimentally affects the animal growth, production and reproduction, which culminates in severe economic loss to the livestock farmers. Among the various internal regulators, hypothalamic-pituitary-adrenal (HPA) axis play a primary role in streamlining the adaptive activities of heat stressed domestic livestock.

Therefore, methodologies pertaining to measuring stress level are very crucial for studying animal adaptation and its associated mechanisms. The HPA axis activity is often measured by corticosteroid release as a means to evaluate stress and well-being in animals. Although, the sympatho adrenal medullary system also originates from HPA axis still its products epinephrine and nor-epinephrine are available only for a transient period of time. Therefore, stress levels are primarily measured by the changes associated with HPA axis and its end-product glucocorticoids, has traditionally been the primary means to make inferences about the stress response in animals. Hence, future research efforts are needed to study in depth the functionality associated with HPA axis at cellular and molecular level to establish the hidden intricacies of stress pathways. These efforts may yield suitable biological markers which may be useful in identifying livestock species with superior thermo-tolerance ability to heat stress. Hence, attempt has been made in this opinion paper to project to the readers the significance of HPA axis for having in-depth understanding of the stress pathways in livestock. These efforts are vital as the scientific community battles in its efforts to identify the most suitable breed specific for different agro-ecological zones.

Importance of HPA axis

The adaptive capability of an animal is predominantly determined by the HPA axis and it is considered very essential for animal survival during adverse environmental condition. The HPA axis consists of the hypothalamus, pituitary gland and the adrenal glands and the interaction among these components constitute a major neuroendocrine system that controls the complex adaptive responses of livestock to heat stress. When an animal subjected to heat stress HPA axis receive sensory input from various sense organs and it gets activated through the release of several neurotransmitters and hormones. In order to respond against heat stress, corticotrophin releasing hormone (CRH) are released by the hypothalamus and, CRH stimulates in turn the secretion of adrenocorticotropic hormone (ACTH) from the anterior pituitary, which results in initiating the synthesis of glucocorticoid from the adrenal cortex. The

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level of activation of the HPA axis is primarily determined by the intensity of stress, and acute stress causes the short-term activation of the HPA axis while chronic stress is responsible for the.
prolonged activation resulting in increased secretion of glucocorticoids to control the life sustaining activities. There are several neuroendocrine hormones regulate, pituitary component activation of HPA axis and the corticotrophin releasing factor (CRF) is the most important ACTH regulating factor. The factors produced by the hypothalamic neurons regulate the synthesis of ACTH from the proopiomelanocortin (POMC) of the anterior pituitary. Vasopressin, a hormone synthesized from the hypothalamus helps in the maintenance of HPA axis after repeated stimulation. Furthermore, pro-inflammatory cytokines also play an important role in the regulation of HPA axis. However, glucocorticoid and leptin coordinate together and repress stress axis activity and eventually help in attaining body homeostasis in stressed animals.

Adrenal gland comprises of outer cortex and inner medulla and the adrenal cortex is responsible for the synthesis of glucocorticoids and mineralocorticoids. However, adrenal medulla secretes epinephrine and nor-epinephrine, which are associated with the emergency fight or flight response. The glucocorticoid and mineralocorticoids secreted from adrenal cortex have a very important role in maintaining vital body functions when the animals are exposed to severe heat stress condition.

Glucocorticoids

Glucocorticoids are the primary end product of HPA axis which controls the homeostasis mechanisms in heat stressed animals. Cortisol is the principal glucocorticoid which functions to relieve stress in animals. It is also considered the ideal biological marker for quantifying heat stress response in livestock. Cortisol is involved in controlling several functions to bring back the normalcy of a heat stressed animals. Among the various functions it governs, cortisol was established to have its primary role in governing hepatic gluconeogenesis to supply regular energy for life sustaining activities during stressful conditions in animals. However while doing so, the productive and reproductive potential and the immune response mechanisms are compromised in heat stressed animals.

Mineralocorticoids

Mineralocorticoids are another group of end product from HPA axis which controls the water and electrolyte balance to bring in homeostasis in stressed animals. Aldosterone, the main mineralocorticoid hormone secreted by the zona glomerulosa of the adrenal cortex. It is essential for the resorption of sodium and a large flux of water at the kidney and thereby, maintaining the sodium and potassium balance.

Genes associated with stress (HPA) pathways

When an animal subjected to heat stress, parvocellular neurons of the paraventricular nucleus (PVN) of the hypothalamus release CRH and arginine vasopressin (AVP) into the anterior pituitary through the hypophysial portal system. The CRH and AVP acts on pituitary corticotrophs, through their associated receptors, such as CRHR1, CRHR2, AVPR1A, AVPR1B and AVPR2, stimulate the secretion of ACTH. The ACTH acts on the adrenal cortex to induce the synthesis of glucocorticoids from the zona fasciculata. Glucocorticoids initiate physiological and behavioral responses through glucocorticoid receptors. The NR3C1 is one of the glucocorticoid receptors and the FKBP5 is a co-chaperone of HSP 90 which regulates glucocorticoid receptor. Two glucocorticoid activated receptors, the type I mineralocorticoid receptors and type II glucocorticoid receptors regulate the effects of glucocorticoids.

Glucocorticoid receptors mediate the negative feedback of the HPA axis by inhibiting the secretion of CRH, AVP and ACTH.

What needs to be explored?

The HPA axis plays a significant role in livestock adaptation when exposed to adverse climatic condition. The glucocorticoids and mineralocorticoids are classical products of HPA axis which works in coordination to maintain homeostasis in the stressed animals. Research pertaining to elucidating the stress pathways associated with HPA axis is in infancy state. With the advancement of molecular biotechnological tools such as whole transcriptome analysis, genomewide association studies, genomewide transcriptome studies and next generation sequencing it is possible to elucidate the various pathways which are altered during stressful conditions. These pathways associated candidate genes which control livestock adaptation as well as the pathways associated with compromised production and immune status should be validated using real time PCR. This warrants future research efforts in this line to generate the baseline information to identify appropriate biological markers to reflect the stress level in domestic livestock. These efforts can go on in a long way to evolve a breed with utmost thermo-tolerant capability.