"Genetic Components of Fitness and Adaptation: Body Temperature Regulation".

Introduction

Beef production is unique in that animals are kept in an extensive environment with minimal environmental modifications, unlike what is seen in dairy, swine and poultry production. Thus, cattle are reared in environments that differ remarkably in temperature, humidity, and wind speed which have forced cattle to adapt in order to survive in these diverse environments. Examples of breed adaptation include the Nellore breed in South America which is well suited to tropical environments or the Scottish Highland breed which is well suited to the opposite extreme. As a consequence of this extreme adaptation in one direction, heat or cold tolerant breeds are more sensitive to environmental extremes in the opposite direction. Suboptimal body temperature regulation during periods of extreme temperature events has deleterious effects on multiple aspects of production including growth, feed efficiency, reproduction, and animal welfare (McDowell, 1972; Hahn, 1999). Currently breeders mitigate the risks associated with heat or cold stress by using knowledge of breed strengths relative to heat or cold tolerance but direct selection of animals within breeds is currently not possible.

The investigation of genetic components of environmental (temperature) tolerance or adaptation could allow for the development of novel indicator traits that can aid in the selection for Economically Relevant Traits (ERT) such as fertility, disease resistance, and feed efficiency across varying environments. Furthermore Physiological Indicator Traits (PIT) associated with body temperature regulation, including blood hormones or heat shock protein response, could be used as an indicator for ERT. Alternatively, susceptibility to environmental stress may be decreased by identifying and selecting for animals within a population that have a larger genetic threshold for heat and/or cold extremes, instead of relying on inherent breed differences. Knowledge of genetic components of body temperature could also be used to improve the efficiency and fitness of animals through environmental specific management decisions.

Literature Review

Modes of heat exchange from the animal to the environment:

A beef cow has an average body temperature ranging from 38.55 to 38.6˚C and a rise or fall of 1°C or less in body temperature is sufficient to produce detectable changes in a number of physiological processes (McDowell, 1972). To maintain this temperature in such narrow limits requires sensitive and immediate acting heat exchange mechanisms. An animal is said to be in its thermoneutral zone when it is in a temperature range that requires the least thermoregulatory effort and temperature regulation is achieved by non-evaporative physical processes alone (Hillman, 2009). The thermonuetral zone is bounded by a lower critical temperature and upper critical temperature and once past this point the animal is under heat or cold stress. When an animal is in its thermoneutral zone the variance across animals in body temperature is small and as the temperature exceeds an animal's lower or upper temperature threshold the variance increases due to differences across animals in their ability to cope with heat or cold stress (Hahn *et al.*, 1990). These differences in thermoregulatory ability are manifested through the complex interaction between anatomical, physiological, and behavioral factors, which are dependent on the life stage, nutrition, genetics, previous degree of heat or cold stress, and health of the animal (McDowell, 1972; Hahn, 1999).

Behavior changes are the first mechanism to account for the heat lost or gained. If behavioral changes don't minimize the heat lost or gained, non-evaporative physical processes that involve the exchange of heat between an animal and its environment are used, which include conduction, radiation, and convection. Resistance to conductive (i.e. heat exchange from particle to particle) heat transfer is proportional to the temperature gradients between the core and outer extremities or the outer extremities and environment (Finch, 1986). As an animal increases in weight its ability to dissipate core heat outward decreases linearly and it becomes more susceptible to heat stress while decreasing its susceptibility to cold stress (Finch, 1985). During cold stress conditions an animal is trying to retain its core body heat, while the environment is acquiring it due to the differing temperature gradients. The animal accounts for this loss of heat by increasing its maintenance energy requirements in order to produce extra heat at a rate of 1% for each 1 ˚C reduction in effective temperature below its lower threshold temperature (Hicks, 2007). In heat stress conditions convection (i.e. heat exchange through a liquid or gas) is accomplished by the redirection of blood flow to the extremities or lungs and its effectiveness is dependent on multiple factors including physical properties of the hair coat and size of the animal. When an animal is first exposed to an adverse environment it reacts initially by activation or acceleration of non-evaporative processes to remain at thermal equilibrium and is defined as short-term adaptive changes (McDowell, 1972; Nienaber and Hahn, 2007). If non-evaporative physical processes fail to keep an animal at thermal equilibrium, evaporative processes take over (McDowell, 1972; Hahn, 1999).

Evaporation is the vaporization of water from the body surface and respiratory tract. Resistance to evaporative heat transfer is a function of the gradient through which the water vapors move (Finch, 1986). Evaporative heat transfer is not dependent on the temperature gradient, which becomes important when the environment is warmer than the animal body temperature and would result in the inward flow of heat from the environment to the animal (Davis *et al.*, 2003). Animal factors that affect the efficiency of evaporative heat loss from the skin surface are sweat gland density, function and morphology, hair coat density, length, and color and regulation of epidermal vascular supply (Carvalho *et al.*, 1995; Collier *et al.*, 2008). A rise in respiratory heat loss through panting is one of the first physical signs of an animal experiencing heat stress (Nienaber and Hahn, 2007).

As a consequence of the animal's inability to regulate its body temperature, inefficient measures commence that involve a decrease in production. One of them being a decrease in feed efficiency due to more energy being used for thermoregulatory processes. Also, a heat or cold stressed animal's immune system becomes suppressed and their cellular proteins lose their structure and function causing an increased susceptibility to sickness. These negative consequences cause a decrease in overall growth rate due to energy being used for processes other than growth, which cause an animal to spend more days on feed. Lastly, from a reproductive standpoint, cold or heat stress has deleterious effects on female and male fertility (Hahn, 1999).

After 2 to 4 days of heat or cold exposure, depending on the individual animal and the degree of heat or cold exposure, mobilization of heat dissipation or retention functions (physiological coping) has progressed to the point that acclimation is apparent (Hahn *et al.*, 1990). Phenotypic acclimation is defined as the "within lifetime phenotypic response" to environmental stress and is a homeorhetic process driven by the endocrine system (Collier *et al.*, 2008). An animal can attain heat or cold tolerance through previous generations of artificial/natural selection or within its lifetime by using alternative pathways that have varying penalties on productivity.

Historically, heat tolerant research has involved comparing and understanding the phenotypic and genetic differences within and between heat-tolerant *Bos indicus* cattle and heat-intolerant *Bos taurus* cattle in controlled or natural environments (Finch, 1985; Finch, 1986; Brown-Brandl *et al.,* 2004; Gaughan *et al.*, 2009). Previous cold tolerance research was concerned with understanding the effects of adverse cold conditions on various production traits using cold tolerant *Bos taurus* cattle (Young, 1983; Hicks, 2007). Multiple indicator traits taken at a single time point or across multiple time points have been used to assess the ability of an animal to regulate its body temperature in extreme hot or cold environments. Some examples include panting score, tympanic temperature, respiration rate (Gaughan *et al.*, 2009), rectal temperature, sweating rate (Finch, 1986), radiotelemetry (Lefcourt and Adams, 1996; Lefcourt and Adams, 1998) and dry matter intake (DMI) (Young, 1983). Due to the fact that body temperature is a continuous function of time, multiple measurements need to be taken to fully describe the circadian rhythm of cattle. Under conditions of minimal heat stress the rhythm is similar across animals, but as the animal is under heat or cold stress the phase, mean temperature, and amplitude get disrupted and the degree of disruption is animal specific (Lefcourt and Adams, 1996; Lefcourt and Adams, 1998).

The degree of disruption can be quantified on an individual animal basis and used as a means of selection by using various phenotypes that indicate the degree of heat or cold stress. Within herd selection for decreased susceptibility to heat or cold stress would broaden the temperature threshold for a herd, which in turn would reduce the occurrence of the deleterious effects during heat or cold stress conditions. This was looked at by Gaughn *et al.* (2009) using panting score along with a heat load index to score individual animals on their ability to cope with heat stress. This approach can be problematic given that an animal's tolerance threshold can be influenced by many non-genetic factors, making it difficult to isolate specific genetic differences in thermoregulatory ability based solely on phenotypic measurements (Scharf *et al.*, 2010). Furthermore, it is a challenge to attain phenotypes that measure the ability of an animal to cope with head or cold stress in a production setting.

An alternative approach would be to isolate genetic variants causing animals within a population to be less sensitive to heat or cold extremes using a component of body temperature as a phenotype. An example of this is illustrated by Howard *et al.* (2011) who found that a genotype by environment interaction existed between the myostatin mutation and a component of body temperature during periods of extreme winter and summer weather conditions. It was found that during heat stress conditions homozygote normal animals were numerically more sensitive to increased environmental temperatures in comparison to animals that were homozygote for the myostatin mutation. Alternatively during cold stress conditions animals that were homozygote for the myostatin mutation were numerically more sensitive to decreased environmental temperatures in comparison to homozygote normal animals (Howard *et al.* 2011).

Knowledge of a gene having variable effects on the phenotype depending on the environment would be beneficial for cattle feeders to implement management strategies based on the genotype of the individual/group. Additionally, breeders can select for genotypes that have increased levels of fitness given the predicted production environment of their customers or own location. The methodology used by Howard *et al.* (2011) can be transferred to other genetic variants or genetic backgrounds that are more conducive to mainstream US beef production and the results could be used to select or better manage cattle based on their genetic temperature threshold.

Genetic parameters for body temperature and relationship to other production traits:

The heritability of various indicators of body temperature regulation during periods of heat stress has been heavily studied in tropical adapted breeds while minimal research has been conducted during cold stress conditions. Burrow (2001) found a heritability of 0.17 for repeated measurements of log transformed rectal temperature on a composite breed of tropical cattle when ambient temperatures exceeded 30˚C. In the same study a favorable genetic and phenotypic relationship was found between rectal temperature and weights and period weight gains from -0.08 to -0.49 and -0.05 to -0.20, respectively. Low to moderate favorable genetic relationships between rectal temperatures and pregnancy status of first 3 parities (-0.16) and days to calving once the bull entered (0.16) has been shown to exist (Burrow, 2001). Turner (1984 and 1982) found a heritability of 0.33 and 0.25 in Bos *indicus*, Bos *taurus* and crossbred lines for repeated measurements of log transformed rectal temperature when the daily maximum ambient temperature was approximately 30˚C. A highly favorable genetic correlation (-0.76) between log transformed rectal temperature and fertility, measured as success or failure in producing a calf at term has been shown to exist (Turner, 1982). Da Silva *et al.* (1973) found heritability estimates for the tropically adapted Canchin breed of 0.11   0.16) and 0.44   0.27) for initial and increase in rectal temperature during a heat stress event. Mackinnon *et al.* (1991) found a heritability of 0.19 for Bos *indicus*, Bos *taurus* and crossbred lines on a single record rectal temperature when the daily maximum ambient temperature was approximately 30˚C. From these studies it has been established that there is a genetic component to the ability of an animal to regulate its body temperature (h^2 of 0.11 to 0.44) through the use of various indicator traits. The genetic correlation between components of body temperature regulation and ERT were favorable, suggesting measures of body temperature could serve as useful indicators to improve various ERT.

Use of genomics in the improvement of quantitative traits in beef cattle:

The traits of economic importance in beef cattle are for the most part quantitative or complex in nature. The classical model of quantitative traits states the phenotypic value is controlled by an infinite number of genes each with an infinitesimal effect as well as by non-genetic or environmental factors (Fisher, 1930). Under this model it is nearly impossible to establish the genotypes of all loci that affect a trait thus a prediction of the total effect of all the genes an animal carries is calculated (estimated breeding value). Traditionally, predictions have been based on the use of dense phenotypes containing the animals and relatives with prior knowledge of the heritability for the particular trait. This approach has been effective and tremendous genetic and phenotypic gains have occurred for a number of economically relevant traits.

This reliance on dense recording of phenotypes is not the most effective for traits that are sex specific (milk yield), measured late in life (longevity), expensive to measure (e.g. methane production, disease resistance, etc.), can only be measured after harvest (meat quality), or have a low heritability (fertility) (Dekkers and Hospital, 2001). In order to increase the accuracy of selection for these traits based on traditional selection schemes requires progeny or sib-testing practices, which increases the generation interval. For these particular traits the accuracy of selection can be increased and generation interval decreased by the use of genomic information to supplement traditional information, which in turn will increase the annual rate of genetic change (Meuwissen *et al.,* 2001). Since the ability to regulate body temperature during hot and cold conditions is difficult and expensive to measure it serves as a trait that would benefit from selection based on genomics. Genomics can be used to locate genomic regions within a population that make an animal less sensitive to heat or cold extremes and then select individuals based on the marker-(s) identified.

The sequencing of the bovine genome uncovered a large number of single nucleotide polymorphisms (SNP), which allowed dense high-throughput genotyping platforms to become commercially available. The use of this information via SNP assays of varying sizes (i.e. 384, 50K, etc.) has allowed for genomic predictors such as Molecular Breeding Values (MBV) to be estimated. MBV for traits where phenotypes are collected on a regular basis (i.e. birth, weaning and yearling weight) has been integrated into National Cattle Evaluation (NCE) for some breeds with others rapidly working towards this end. The challenge lies in the development and implementation of genomic selection (GS) for traits where the phenotype is not measured on a regular basis. Unfortunately, many of these traits (fertility, feed efficiency, adaptation, disease resistance) are of paramount importance to the beef industry. Genomic information used to enhance traditional NCE will become more important in the future to aid in developing selection tools for novel traits as those listed above where phenotypic data is sparse at best.

This technology can be transferred to aid in the management of cattle. This is known as Marker-Assisted Management (MAM) and it consists of using the results of DNA-marker tests to predict future phenotypes of the animal being tested and sort individual cattle into management groups that are most likely to achieve specific endpoints (Van Eenennaam, 2012). This allows cattle feeders to more efficiently optimize carcass endpoints (i.e. target backfat, weight or quality grade) by deciding how long to feed or whether to use growth-promoting technologies on a group of animal's based on genomic information. Another viable option for MAM is to optimize individual animal fitness by placing animals in an environment that matches up with their upper and lower threshold temperature. MAM allows improved feedlot efficiency by placing animals in a location and feeding them at a specific time of year based on their temperature threshold, which results in faster growth rate and increased feed efficiency due to less energy being used for thermoregulatory processes.

Economically Relevant Traits and Physiological Indicator Traits:

The vast majority of EPD computed in NCE today do not directly affect profit, but are correlated with traits that affect profit. As an example, birth weight and scrotal circumference are measured not because a producer gets more or less money for the weight of his cattle at birth or the scrotal circumference of his bulls, rather these indicator traits are used to indicate the genetic merit of an animal for another trait, in this case calving ease and daughter age at puberty (Golden *et al.*, 2000). The traits we are trying to improve and that are directly associated with a specific cost of production or an income stream are labeled as economically relevant traits (ERT) (Golden *et al.*, 2000). Examples of ERT include heifer pregnancy rate, sale weight, or cow maintenance feed requirement. The importance of indicator traits to predict the genetic merit of ERT is realized for ERT that are unobservable, difficult to obtain/identify a phenotype, expensive to measure, or has a low heritability and the indicator trait is genetically correlated with the ERT. The efficacy of selection is improved by the increase in accuracy for the ERT, which in turn increases the rate of genetic improvement (Golden *et al.*, 2000).

A way to quantify the genetic superiority of an individual for a complex ERT is to combine a suite of practical phenotypes with the proper weighting that accurately predict the ERT. A reductionist approach to improving complex traits allows for the use of practical phenotypes that together may explain the ERT that is highly accurate and robust. Examples of practical phenotypes include traits that can be measured early in life, are inexpensive to measure, have a higher heritability then the ERT, and are genetically correlated with the trait of interest. An additional approach would be to use physiological indicator traits (PIT) or traits that are expected to be closely related to physiological processes that are components of the trait of interest (Thallman, 2008). This approach takes advantage of the fact that genes related to the physiological process have genetic polymorphisms that affect the ERT and selection for these will in turn positively impact the trait of interest. Potential PIT could be processes that are associated with body temperature regulation (i.e. Heat Shock Proteins, hormone levels, etc.), disease resistance (i.e. red blood cells, or immunological blood factors, etc.), and feed efficiency (hormone levels, enzyme levels, etc.). Another benefit of developing genomic selection tools for PIT is that they could be measured with less error as compared to complex phenotypes such as feed efficiency or fertility, potentially allowing for genomic predictors of high accuracy for PIT.

Conclusions and Implication to Genetic Improvement of Beef Cattle

Suboptimal body temperature regulation has been shown to have negative effects on efficiency of production including growth, feed efficiency, reproduction, and animal welfare (McDowell, 1972; Hahn, 1997). The vast diversity between breeds in their ability to cope with heat or cold stress and the deleterious effects of suboptimal body temperature regulation on multiple economic production traits suggest that inherent differences in body temperature regulation could serve as useful indicator traits to improve the adaptation of animals and efficiency of beef production. Decreased sensitivity to thermal stress events allows for high levels of production to be sustained in the midst of extreme stress events which have positive affects in all areas of production.

The response of animals during times of extreme temperature stress events can be used as an indicator trait to improve ERT across varying environments. PIT associated with body temperature regulation, including blood hormones or heat shock protein response, can be used as an indicator trait in tandem with others in order to estimate the genetic value of an individual for a complex ERT that is a combination of multiple production traits. Knowledge of an animal's genetic threshold paves the way for the implementation of cold or heat stress management practices. Based on an animal's genetic makeup, it could be determined that they would excel if placed on feed in a given region during a specific time of year.

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