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Genotype-by-environment interaction for yearling weight of Nellore cattle in pasture and feedlot conditions using a "double" genomic reaction norm model

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Abstract

In many tropical climate countries, beef cattle are typically raised in extensive pasture-based systems and exposed to harsh environmental conditions. A portion of these animals is then confined for 3 to 4 mo prior to slaughter. Thus, the main objectives of this study were to estimate variance components and genetic parameters to assess the level of genotype-by-environment interactions (G×E) in Nellore cattle raised on pasture until weaning and finished in feedlot conditions, evaluate genetic trends, and perform a genome-wide association study to identify genomic regions associated with the animals' responses to different production environments. We analyzed the body weight measured at approximately 378 d of age (W378) of 5,070 Nellore males from an experimental herd. The heritability estimates for W378 varied considerably between pasture and feedlot environments (0.33 ± 0.05 to 0.62 ± 0.05), indicating potential differential responses to selection across environments. Overall, the genetic correlation estimates for W378 across environments were high (>0.80) but reached values around 0.60 between certain levels of pasture and feedlot environments (e.g., "good" pasture vs. "poor" feedlot and vice versa). Reaction norms for sires and single nucleotide polymorphism highlighted the existence of G×E, showing divergent genetic responses to pasture and feedlot conditions. Genetic trends revealed a gradual improvement in feedlot environments at the cost of reduced performance in optimal pasture conditions, indicating a moderate genetic antagonism. Genomic regions explaining significant percentage (1% to 11%) of the total additive genetic variance for responses to pasture and feedlot were identified, with distinct loci contributing to the genetic architecture of W378 in each environment. Therefore, G×E between pasture and feedlot environments should be considered in breeding programs. The genomic regions identified provide potential targets for further exploration to enhance beef cattle performance across production system conditions.

Lay Summary

In tropical regions, beef cattle are typically raised on large pasture areas and are exposed to various environmental challenges, including limited or low-quality nutrition, heat, and disease pressure. A portion of these animals is later moved to feedlots, where they are fed more intensively for 3 to 4 mo before being slaughtered. In this context, this study aimed to assess how genetic factors affect yearling weight in Nellore beef cattle under 2 different environments: pasture and feedlot. We used a statistical model, called the "double" reaction norm model, to understand how the same animals respond genetically to these 2 environments. The results showed that while cattle selected for higher performance in feedlots improved over time, their performance in pasture environments declined. We also identified important regions of the cattle genome that influence these environmental responses, which can help the refinement of breeding programs aiming to improve the performance of beef cattle in diverse production systems. These findings emphasize the need for breeding programs to consider performance across environments in genetic improvement programs.

Key words: genetic antagonism, genetic correlation, genotype-by-environment interaction, GWAS, reaction norm

Abbreviations: CG, contemporary group; GEBV, genomic estimated breeding values; G × E, genotype-by-environment interaction; GWAS, genome-wide association study; NeC, Nellore control line; NeS, Nellore selection line; NeT, Nellore traditional line; W378, body weight at around 378 d of age; SNP, single nucleotide polymorphism

Introduction

In tropical climate regions, beef cattle are typically raised in large pasture areas and exposed to nutritional, thermal, and health challenges. Usually, Zebu cattle (*Bos taurus indicus*) are kept on pasture until around 18 to 21 mo of age, which corresponds to more than 80% of their lifespan. A portion of these animals is then confined in feedlots for 3 to 4 mo and slaughtered between 21 and 25 mo (Ferraz and Felício, 2010). Although feedlot systems tend to alleviate nutritional challenges, these animals may still experience issues

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related to health, thermal conditions, or other stressors (Blakebrough-Hall et al., 2022; Maia et al., 2023; Romanello et al., 2023).

Many beef cattle animals are exposed to these 2 environments during their lives (pasture vs. feedlot). These environments require specific physiological and behavioral responses from the animals. Therefore, their performance is expected to differ across environments. From a genetic improvement perspective, there is a need to assess if animals that are genetically selected to perform well in pasture environments are also the best performers under feedlot conditions, and vice versa.

As noted by Raidan et al. (2015), genotype-environment interaction (G×E) can be an important issue in the selection of beef cattle raised or finished in pastures or feedlots. Raidan et al. (2015) reported genetic correlations different from unity for the same traits (average daily gain and final weight) in Nellore young bulls tested on pasture or in feedlots. Similarly, Ling and Hay (2024) found moderate evidence of G×E between feedlot conditions and native rangelands with nutritional supplementation for improving the body condition score of composite cattle. These authors emphasized that there is sufficient genetic variation to enable the selection of animals better suited to pasture environments with lower supplemental feeding costs. In addition, GxE have been reported for a wide range of traits and environments in beef cattle (Silva Neto et al., 2023, 2024). Therefore, the primary objective of this study was to evaluate how the genetic potential for yearling weight in Nellore beef cattle changes as a function of the environments (pasture vs. feedlot) based on a "double" genomic reaction norm model. More specifically, we estimated variance components and genetic parameters (e.g., heritability and genetic correlations) to assess the level of G×E in Nellore animals raised on pasture until weaning and finished in feedlot conditions, evaluated genetic trends, and performed genome-wide association study (**GWAS**) to identify genomic regions associated with the animals' responses to different production environments.

Material and Methods

The farm where the data was collected followed all animal welfare guidelines established by the law No. 11.977 from the state of São Paulo, Brazil. All the datasets analyzed were obtained from an existing database and approval of the Ethics Committee was therefore not necessary.

Phenotypes and pedigree

The data used in this study were obtained from the APTA Beef Cattle Center Institute of Animal Science, Sertãozinho, São Paulo, Brazil (21°10'S and 48°50'W). Phenotypes of Nellore males born between 1981 and 2022 were used, along with a pedigree file that included 8,636 individuals. The animals were raised on pasture (*Panicum maximum* and *Brachiaria brizantha*) and weaning occurred when the calves reached approximately 7 mo of age. After weaning, all animals (on average 120 per year) were confined for 168 d in paddocks measuring 3,600 m^2, with feed provided ad libitum twice a day. Feed included corn silage, hay, soybean meal, ground corn, and mineral salt with urea. At the end of the feedlot period, the animals were weighed at approximately 378 d of age (W378).

The experimental selection program for the Nellore population studied here started in 1976, intending to increase the yearling weight of animals based on individual performance. In 1980, the Nellore population was divided into 3 selection lines: Nellore Control (NeC), Nellore Selection (NeS), and Nellore Traditional (NeT). The NeC line is a closed line in which sires from the same program were used, and the animals were selected for average yearling weight. In the other 2 lines, NeS and NeT, the animals were selected for the highest differentials to increase yearling weight. While the NeS and NeC lines are maintained as closed lines, the NeT line has received sires from the 2 other lines and from commercial herds. The average additive genetic relationship between NeC and the other lines was 0.007, while the relationship between NeT and NeS was reported to be 0.053 (Cardoso et al., 2018). The NeT line has been additionally selected for the lowest differentials of residual feed intake since 2012. More details about the experimental selection program can be found in Mercadante et al. (2003) and Cardoso et al. (2018).

Contemporary groups (**CG**) were defined based on selection line, year, and month of birth. The CG with fewer than 5 records, and records deviating 3.5 standard deviations (**SDs**) from the phenotypic mean of the respective CG were excluded from further analyses. A summary of the data structure for W378 is provided in Table 1.

Table 1. Summary of the data structure for body weight measured at around 378 d of age in Nellore cattle according to the selection line (Nellore Control—NeC, Nellore Selection—NeS, and Nellore Traditional—NeT)

Item	NeC	NeS	NeT
Number of animals in the pedigree file	1,767	2,717	3,807
Number of animals with phenotypic records	1,103	1,732	2,235
Number of genotyped animals with phenotypic records	253	488	837
Number of sires with progeny with phenotypic records	115	156	199
Number of genotyped sires with progeny with phenotypic records	24	60	83
Number of dams with progeny with phenotypic records	562	785	998
Number of genotyped dams with progeny with phenotypic records	99	243	327
Number of recorded progeny from genotyped sires	219	693	1,087
Number of recorded progeny from genotyped dams	192	497	646
Number of contemporary groups	106	121	124
Phenotypic mean of the trait (Standard deviation), kg	282.92 (32.82)	335.55 (46.91)	335.48 (47.22)
Maximum phenotypic value of the trait, kg	409.41	503.63	512.29
Minimum phenotypic value of the trait, kg	176.26	123.7	135.71

Genotypes

A total of 3,350 genotyped individuals were used in this study, including 1,579 males with phenotypes and their relatives. The animals were genotyped using single nucleotide polymorphism (**SNP**) panels of different densities over the years (Illumina BovineHD BeadChip, San Diego, CA, USA, $n = 780$; GeneSeek Profiler 75K—Indicine, Lincoln, NE, USA, $n = 1{,}318$; GGP Indicus 50K, Lincoln, NE, USA, $n = 1{,}252$). Animals genotyped with medium-density SNP panels were imputed to a high-density (**HD**) SNP panel containing approximately 770K SNP markers, using a reference population of 6,862 animals genotyped with the HD SNP panel and the software FImpute v3 (Sargolzaei et al., 2014).

The criteria considered for genotype quality control were 1) inclusion of only autosomal SNP with a GenCall score greater than 0.80; 2) removal of SNP with a minor allele frequency ≤ 0.05; 3) removal of SNP and samples with a call rate ≤ 0.90; 4) removal of SNP with extreme deviation from Hardy–Weinberg equilibrium (P-value $\leq 10^{-5}$); 5) removal of SNP with duplicated or unknown positions; and 6) removal of SNP or samples with Mendelian conflicts. After the genomic quality control, 3,350 animals and 383,739 SNP markers remained in the database for subsequent analyses.

Environmental descriptor of pasture and feedlot

In reaction norm models, it is common to adopt a 2-step approach (Strandberg et al., 2002; Cardoso & Tempelman, 2012) in which 1) a regular model is used to obtain CG solutions (Best Linear Unbiased Estimates – BLUE); and, 2) the CG solutions are used as known covariate values (environmental descriptors) in reaction norm models. As stated by Cardoso & Tempelman (2012), the CG represents the most basic descriptor characterizing beef production environments. To describe the quality of the pasture and feedlot environments experienced by the animals, 2 environmental descriptors were adopted: the first was based on the animals' performance for weaning weight, which was recorded at the end of the pasture period. The second descriptor was based on W378, which was recorded at the end of the feedlot period. A single-trait animal model was employed to analyze each of these traits separately. The regular animal models included the direct additive genetic effect, maternal additive genetic effect (except for W378), maternal permanent environmental effect (except for W378), systematic effects of CG, animal's age at measurement (linear effect), dam's age at calving (fitted as linear and quadratic covariates), and the random residual effect. Thus, all animals included in the study were associated with 2 environmental descriptors: solutions (BLUE) for the CG effect of weaning weight (pasture phase) and W378 (feedlot phase). Specifically, weaning weight was used solely to describe the pasture environment in step 1 of the reaction norm model. In contrast, W378 was used both as an environmental descriptor for the feedlot phase (step 1) and as the target trait for genetic parameter estimation (step 2, as described in the next section).

Since the environmental descriptors exhibited scale differences and the studied herd comprised 3 selection lines, we separately standardized each environmental gradient descriptor's values to a mean of 0 and a SD of 1 within each selection line. Standardization within each selection line was necessary because animals from the selected lines (NeT and NeS) showed higher average performance for W378 compared to NeC. These phenotypes from the selected lines led to higher CG solutions, and environments were erroneously considered better for NeT and NeS animals compared to NeC (Fig. S1). However, the 3 selection lines were maintained under approximately the same environmental conditions. The importance of standardizing environmental descriptors to avoid bias from known factors was discussed and employed by Pegolo et al. (2011) and Santana et al. (2024). Additionally, to avoid a small number of records in any of the levels of each environmental descriptor, we created 16 classes of 0.25 SDs (−1.875 to +1.875). Values above +1.875 or below −1.875 SDs were grouped. The distribution of W378 records across the classes of environmental descriptor values is shown in Fig. 1.

Effect of pasture and feedlot environment on the phenotypic scale of W378

To illustrate the impact of different production environments (pasture and feedlot) on animal performance, we obtained least square means for W378 using a simple linear model that included the effect of selection line, production environment class according to the number of SD from the mean of the environmental descriptors—1) ≤0 SD "poor" pasture, ≤0 SD "poor" feedlot; 2) ≤0 SD "poor" pasture, >0 SD "good" feedlot; 3) >0 SD "good" pasture, ≤0 SD "poor" feedlot; 4) >0 SD "good" pasture, >0 SD "good" feedlot—, age at measurement as a linear covariate, dam's age at calving as linear and quadratic covariates, and the residual effect.

"Double" reaction norm to model genetic responses of W378

As our main objective was to assess the genetic response of animals for W378 to pasture and feedlot environments, we employed a single-step genomic reaction norm model using the 2 environmental descriptors (pasture and feedlot) presented in the previous section (step 2). The reaction norm model can be described as follows:

$$\mathbf{y} = \mathbf{X}\beta + \mathbf{Z}_{\mathrm{i}}\mathbf{d}_{\mathrm{i}} + \mathbf{Z}_{\mathrm{s-P}}\mathbf{d}_{\mathrm{s-P}} + \mathbf{Z}_{\mathrm{s-F}}\mathbf{d}_{\mathrm{s-F}} + \mathbf{e},$$

where, $\mathbf{y}$ was the vector of observations; β was the vector of systematic effects of CG (as previously defined), age at

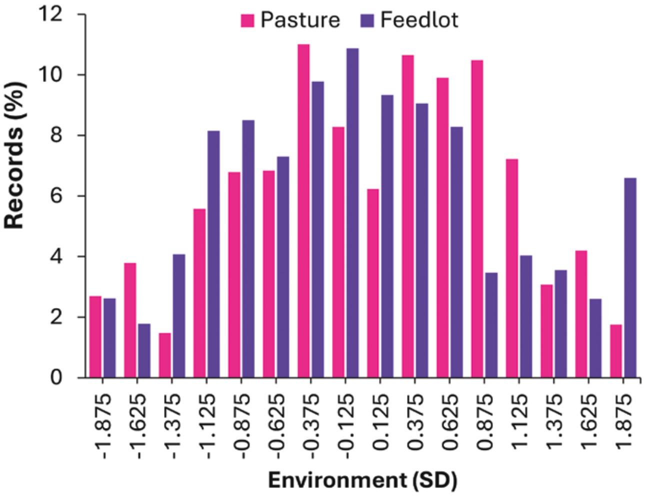

Figure 1. Distribution of body weight records at approximately 378 d of age (W378) in Nellore cattle (selection lines: Nellore Control—NeC, Nellore Selection—NeS, and Nellore Traditional—NeT) according to the pasture and feedlot environments (in standard deviations, SD).

measurement as a linear covariate, dam's age at calving as linear and quadratic covariates; $\mathbf{d_i}$ was the vector of direct additive genetic intercept of the reaction norms; $\mathbf{d_{s-P}}$ was the vector of direct additive genetic slopes of the reaction norms for pasture environments; $\mathbf{d_{s-F}}$ was the vector of direct additive genetic slopes of the reaction norms for feedlot environments; and $\mathbf{e}$ was the vector of residual effects. A heterogeneous residual variance structure was adopted with 4 classes according to the number of SD from the mean of the environmental descriptors as described in the previous section. The incidence matrices $\mathbf{X}$, $\mathbf{Z_i}$, $\mathbf{Z_{s-P}}$, and $\mathbf{Z_{s-F}}$ link phenotypic records to their corresponding systematic effects, the direct additive genetic intercept, and the direct additive genetic slopes for pasture and feedlot environments, respectively. The following covariance structure was assumed for the estimation of (co)variance components:

$$\begin{bmatrix} \mathrm{d_i} \\ \mathrm{d_{s-P}} \\ \mathrm{d_{s-F}} \end{bmatrix} \sim \mathrm{N}\left(0, \begin{bmatrix} \sigma^2_{\mathrm{d_i}} & \sigma_{\mathrm{d_{is-P}}} & \sigma_{\mathrm{d_{is-F}}} \\ \sigma_{\mathrm{d_{is-P}}} & \sigma^2_{\mathrm{d_{s-P}}} & \sigma_{\mathrm{d_{ss-PF}}} \\ \sigma_{\mathrm{d_{is-F}}} & \sigma_{\mathrm{d_{ss-PF}}} & \sigma^2_{\mathrm{d_{s-F}}} \end{bmatrix} \otimes \mathbf{H} \right),$$

where, $\mathrm{d_i}$, $\mathrm{d_{s-P}}$, and $\mathrm{d_{s-F}}$ represented the direct additive genetic intercept (i) and slope (s) for the pasture (P) and feedlot (F) effect, respectively; $\sigma^2_{\mathrm{d_i}}$ represent the intercept variance for the direct additive genetic effect; $\sigma^2_{\mathrm{d_{s-P}}}$ and $\sigma^2_{\mathrm{d_{s-F}}}$ represent the additive genetic slope variances for pasture and feedlot, respectively; $\mathbf{H}$ was the matrix that combines pedigree and genomic information (Aguilar et al., 2010); and ⊗ was the Kronecker product. Once there is an estimate of $\hat{\mathbf{G}}$ (3×3 covariance matrix as described above), the covariance function model can be used to calculate variances and covariances of interest across different environmental points. For instance, the additive genetic (co)variance estimates ($\mathbf{V_P}$) of W378 in pasture environments are given by:

$$\boldsymbol{V_P = \phi_P \widehat{G}_P \phi'_P},$$

where, $\boldsymbol{\Phi_P}$ is a 16×2 matrix consisting of a column of ones and a second column representing pasture environments, with values ranging from −1.875 to +1.875 SDs; and $\mathbf{G_P}$ is a 2×2 matrix that includes the estimates of variance components for the intercept ($\sigma^2_{\mathrm{d_i}}$), pasture environment ($\sigma^2_{\mathrm{d_{s-P}}}$), and the covariance term ($\sigma_{\mathrm{d_{is-P}}}$). Similarly, the genomic estimated breeding value (**GEBV**) of an individual, based on the reaction norm model, can be calculated as:

$$GEBV_k = [1\ P_l\ F_m]\,\hat{\mathbf{u}}_\mathbf{k}$$

where, the elements $\mathrm{P_l}$ and $\mathrm{F_m}$ represent the pasture and feedlot environments, respectively; and $\mathbf{u_k}$ is a vector for the estimated regression coefficients for animal k corresponding to the intercept, pasture slope, and feedlot slope. Further details on random regression models can be found in Schaeffer (2016) and Oliveira et al. (2019).

Using the Gibbs sampler, conditional Gaussian distributions of systematic effects, breeding values, and inverted Wishart distributions for genetic and residual (co)variances were sampled. Chains consisting of 150,000 samples, a burn-in of 50,000 samples, and a thinning interval of 25 were used. Convergence was visually assessed using trace plots to evaluate the mixing of the chains. The remaining 4,000 samples were utilized to compute the (co)variance components and genetic parameters. All the analyses were performed using the BLUPF90 family of programs: GIBBSF90+, PREGSF90, and POSTGSF90 (Misztal et al., 2014).

GWAS

The SNP effects of the slopes for pasture and feedlot of the reaction norms were estimated using the weighted single-step GBLUP method (with 2 iterations) proposed by Wang et al. (2012). The percentages of the total additive genetic variance explained by moving genomic windows of 20 adjacent SNP were computed. Genomic windows that explained at least 1% of the total additive genetic variance for the slopes were considered as potentially associated with the specific response of animals to changes in the pasture and feedlot environments. Genes within the candidate genomic regions were annotated considering an upstream and downstream interval of 200 kb using the Ensembl Biomart (release 112, www.ensembl.org/index.html) and the ARS-UCD1.3 bovine genome assembly (Harrison et al., 2024). Furthermore, the QTLdb database (www.animalgenome.org/cgi-bin/QTLdb/BT/index; Hu et al., 2022) was explored to determine if any candidate genomic region had been previously reported as quantitative trait loci in cattle. The biological processes and molecular functions of candidate genes were annotated using the PANTHER Classification System (Thomas et al., 2022).

Genomic reaction norms and SNP effects

To illustrate G × E, GEBV were obtained for sires with at least 10 progeny records in "poor" (−1.875 SD) or "good" (+1.875 SD) environments for both pasture and feedlot. Additionally, we selected the top 1% of SNP (n = 3,838) with the highest absolute effect on each term of the reaction norm model (intercept, slope for pasture, and slope for feedlot). Based on this sample, SNP shared between the slope for pasture and the slope for feedlot, but not shared with the intercept, were identified and their estimated genomic reaction norms were presented. In addition, SNP associated with the intercept and not related to the slope terms of the reaction norms were sampled. This was done to investigate potential SNP-by-environment interactions and to determine whether SNP are related specifically to responses in different environments, rather than to the overall level of performance, and vice versa.

Genetic trends

We assessed the means of solutions for the intercept and slopes for both pasture and feedlot environments according to the animals' year of birth over the past 30 yr (1993 to 2022). This procedure was conducted by selection line to evaluate potential impacts of selection practices on the environmental sensitivity of animals in the studied population. To ensure the reliability of the trends, we included only animals with their own phenotypic records and/or those with progeny having recorded performance data.

Results

Effect of pasture and feedlot environment on the phenotypic scale of W378

Important differences in animal performance were observed based on the combination of pasture and feedlot production environments (Fig. 2). Notably, better pasture environments combined with good feedlot environments resulted in optimal performance. Conversely, a poor pasture environment combined with a good feedlot environment led to better performance for W378 than the opposite situation. The Pearson correlation between the pasture and feedlot standardized environmental descriptors was 0.64.

(Co)variance components and parameters related to G × E

The mean estimates of the additive genetic variance for the slope of the reaction norms in the pasture (73.180) and feedlot (68.107) environments were relatively similar with overlapping posterior density intervals (Table 2). The genetic covariances between the intercept and each of the 2 slope terms of the reaction norms exhibited opposite signs. Consequently, divergent genetic correlations were observed between the intercept and the response to the pasture environment (−0.463) and feedlot environment (0.408). The posterior mean of the genetic correlation between the slopes of the reaction norms was moderate and negative (−0.382). The posterior means of the residual variances for poor pasture environments were slightly higher than those obtained for good pasture environments. The opposite was observed for feedlot environments, where combinations of good environments showed higher mean residual variance than poorer environmental conditions.

The ratios between the variance of the slopes and the intercept were calculated to assess the degree of G × E for W378. A significant magnitude of the G × E effect was observed in response to both pasture and feedlot environments. The G × E for the pasture environment was slightly higher (0.204) than for the feedlot environment (0.189).

Heritability and genetic correlation according to pasture and feedlot environments

The posterior mean estimates of heritability for W378 were 0.44. Heritability estimates showed notable variations across the values of the environmental descriptors for pasture and feedlot environmental gradients, as illustrated in Fig. 3. The overall mean heritability estimates were 0.39 for W378 in poorer feedlot environments (Fig. 3, left side) and 0.58 for more favorable feedlot environments (Fig. 3, right side). For pasture environments, higher overall mean heritability estimates were observed in extremely poor environments (0.62), a decrease in intermediate environments (0.33), and a slight increase in more favorable environments (0.35).

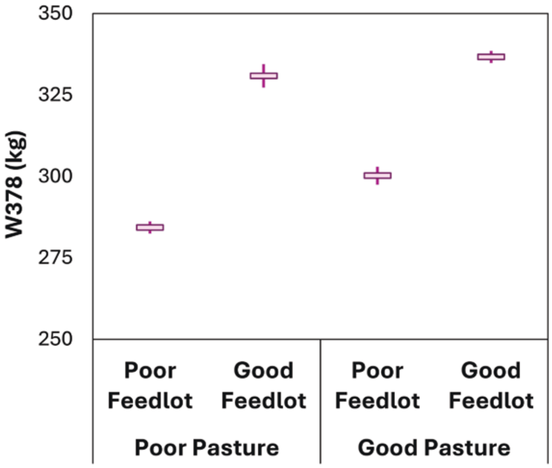

Figure 2. Least squares means (horizontal bars) and 95% confidence intervals (vertical lines) of body weight at approximately 378 d of age (W378) in Nellore cattle according to the pasture and feedlot environments. “Poor” refers to environmental descriptor values for pasture or feedlot that are equal to or below the average, while “Good” refers to values above the average.

The overall mean estimates of genetic correlation for W378 between different combinations of pasture and feedlot environments was 0.79 (Fig. 4). For poor pasture environments combined with different levels of feedlot environments, the overall mean genetic correlation estimate was 0.78. In contrast, for favorable pasture environments combined with different levels of feedlot environments, the overall mean genetic correlation estimate was 0.58. Poor feedlot environments combined with different levels of pasture environments showed a mean genetic correlation estimate of 0.62. Conversely, good feedlot environments combined with different levels of pasture environments exhibited overall mean genetic correlation estimate of 0.76. The overall mean genetic correlation for W378 between intermediate pasture and intermediate feedlot environments was close to 0.90.

Genomic reaction norms and SNP effects

Genomic reaction norms demonstrated G × E for W378 through the reranking of sires between divergent pasture and feedlot environmental conditions (Fig. 5). Among the top SNP ($n = 3{,}838$) for each term of the reaction norm model parameters (intercept, slope for pasture, slope for feedlot), 2.74% ($n = 105$) were shared between the 2 slope terms and not with the intercept of the reaction norms (Fig. 6, left side). Conversely, among the top SNP associated with the intercept, 36.63% ($n = 1{,}406$) were unique and not shared with the slope terms of the reaction norms (Fig. 6, right side).

Genetic trends

Genetic trends showed divergence in the intercept (general performance level) and the specific responses of animals to different environments (slopes), as illustrated in Fig. 7. As expected, the intercepts of the selected lines for higher weight (NeT and NeS) exhibited a strong increase over the analyzed years, while NeC remained approximately constant over time (Fig. 7, left side). The selected lines showed a trend of more negative GEBV for the pasture slope, indicating poorer performance in pasture for W378 (Fig. 7, center). Conversely, the selected lines tended to exhibit more positive GEBV for feedlot environments (Fig. 7, right side), indicating better performance in those environments. NeC showed stable trends for responses to different environments over the years.

GWAS

Five genomic windows explaining at least 1% of the total additive genetic variance for the pasture slope of W378 were identified, with 2 of them located on the *Bos taurus* autosome (**BTA**) 7 (Table 3). Approximately 7.7% of the total additive genetic variance associated with the pasture slope was explained by the combination of the relevant genomic windows. In these regions, 16 candidate genes were annotated. Some of these regions were previously associated with shear force, hip width, and marbling score in beef cattle. In dairy cattle, the identified regions were previously linked to health and locomotion traits (digital cushion thickness, laminitis, sole hemorrhage), productive life, reproduction, milk production, and milk quality. The biological processes identified for

Table 2. Posterior mean, median, and standard deviation (PSD), and 95% highest posterior density interval (HPD95%) of (co)variance estimates obtained based on a reaction norm model fitting body weight measured around 378 d of age Nellore cattle

Parameter[1]	Mean	Median	PSD	HPD 95%	
$\sigma^2_{i_g}$	364.238	362.300	43.226	285.600	454.500
$\sigma^2_{s_g-P}$	73.180	71.505	18.738	39.380	112.050
$\sigma^2_{s_g-F}$	68.107	66.780	21.350	29.090	113.950
σ_{is_g-P}	–74.432	–73.970	19.051	–112.900	–38.040
σ_{is_g-F}	62.149	62.865	22.664	17.340	104.250
σ_{ss_g-PF}	–27.252	–26.535	14.691	–56.945	–1.939
$\sigma^2_e - P_{\text{poor}}F_{\text{poor}}$	622.474	623.700	50.758	520.500	719.700
$\sigma^2_e - P_{\text{poor}}F_{\text{good}}$	848.920	845.050	90.463	676.900	1,033.500
$\sigma^2_e - P_{\text{good}}F_{\text{poor}}$	539.241	537.400	48.748	447.150	636.900
$\sigma^2_e - P_{\text{good}}F_{\text{good}}$	757.205	758.000	45.473	669.850	845.300
r_{is_g-P}	–0.463	–0.465	0.108	–0.664	–0.243
r_{is_g-F}	0.408	0.410	0.153	0.113	0.704
r_{ss_g-PF}	–0.382	–0.386	0.170	–0.684	–0.033
$\sigma^2_{s_g-P}/\sigma^2_{i_g}$	0.204	0.195	0.061	0.106	0.342
$\sigma^2_{s_g-F}/\sigma^2_{i_g}$	0.189	0.183	0.064	0.083	0.330

σ^2 = variance; σ = covariance; i = intercept; s = slope; g = additive genetic effect; P = pasture; F = feedlot; e = residual; r = genetic correlation.

[1] "Poor" refers to environmental descriptor values for pasture or feedlot that are equal to or below the average, while "Good" refers to values above the average.

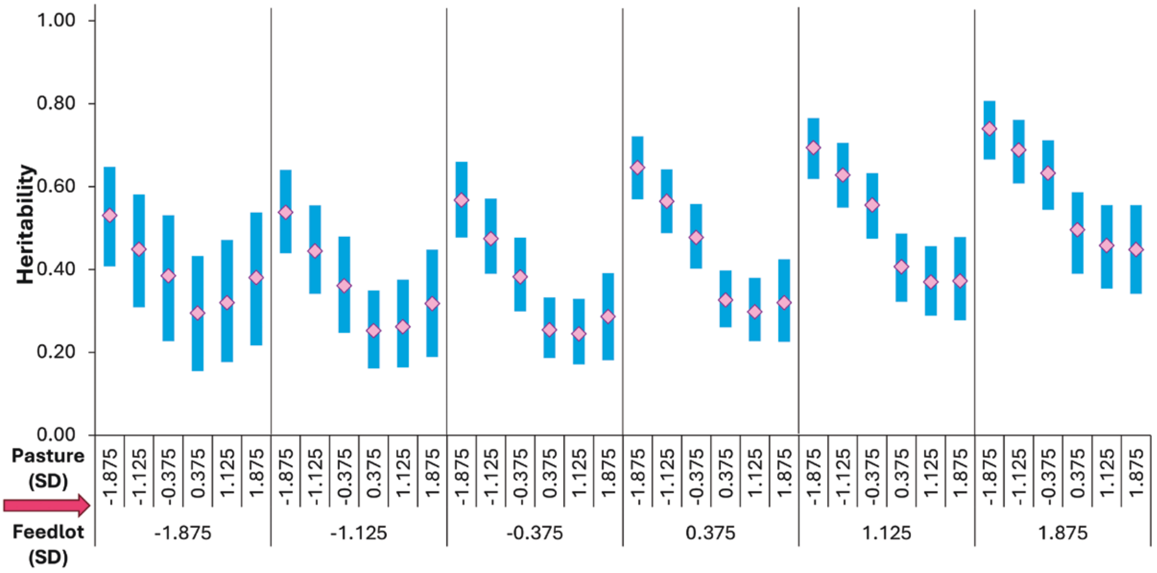

Figure 3. Posterior means (diamond symbols) and 95% highest posterior density intervals (vertical bars) of the heritability estimates for body weight at approximately 378 d of age in Nellore cattle according to the pasture and feedlot environments (in standard deviations, SD).

the pasture slope included cellular process (34.5%), biological regulation (27.6%), metabolic process (13.8%), localization (13.8%), and response to stimulus (10.3%). The molecular function terms identified were binding (45.4%), molecular transducer activity (18.2%), catalytic activity (18.2%), and transporter activity (18.2%).

For the reaction norm slope of W378 in feedlot environments (Table 4), we identified 10 genomic windows explaining at least 1% of the total additive genetic variance compared to the pasture slope. Eighty candidate genes were annotated for these genomic regions. A single genomic window located on BTA10 accounted for over 11% of the total additive genetic variance of the feedlot slope. The combination of the top identified windows explained approximately 30% of the total genetic variance of the feedlot slope. Similar to the pasture slope, genomic regions located on BTA4 and BTA7 harbored important genes for the response to feedlot environments. Some regions identified for the feedlot response were previously associated with various traits in beef cattle, such as body weight, height, weight gain, meat quality, health, and reproduction. In dairy cattle, the most important regions identified were previously associated with reproduction, fertility, productive life, milk yield and quality, and heat tolerance. The biological processes identified for the feedlot

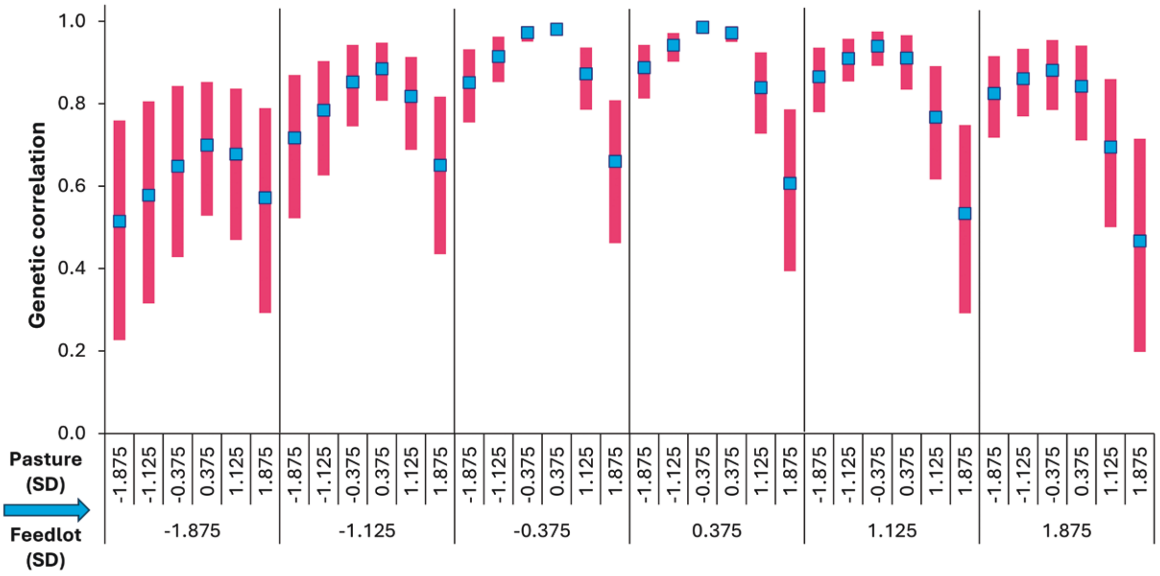

Figure 4. Posterior means (square symbols) and 95% highest posterior density intervals (vertical bars) of the genetic correlations estimates for body weight at approximately 378 d of age in Nellore cattle between different combinations of pasture and feedlot environments (in standard deviations, SD).

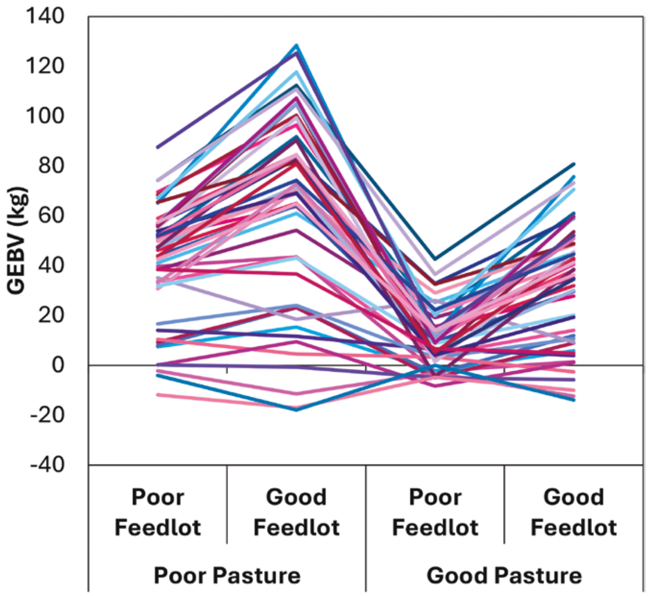

Figure 5. Posterior means of the genomic estimated breeding values (GEBV, reaction norms) of a random sample of 50 sires with at least 10 progeny records for body weight at approximately 378 d of age across different combinations of pasture and feedlot environments.

slope included cellular process (35.8%), biological regulation (17.9%), metabolic process (14.2%), localization (11.3%), developmental process (5.7%), multicellular organismal process (4.7%), response to stimulus (3.8%), reproductive process (2.8%), reproduction (2.8%), and homeostatic process (0.9%). The molecular functions were binding (44.2%), catalytic activity (25%), transcription regulator activity (11.5%), molecular transducer activity (7.7%), molecular adaptor activity (3.8%), molecular function regulator activity (3.8%), and transporter activity (3.8%).

Discussion

Beef cattle production based on a combination of pasture and feedlot environments is a common practice in countries such as Brazil, Argentina, Uruguay, and Australia. The major differences between pasture and feedlot environments can create a potential scenario for the occurrence of G × E in animal performance. Thus, we investigated the genetic responses of W378 in Nellore cattle to different pasture and feedlot environments using a "double" genomic reaction norm model. To our knowledge, this is the first application of this model to beef cattle.

As expected, the combination of optimal pasture and feedlot environments resulted in the best performance for W378 in cattle. However, the combination of poor pasture with superior feedlot environments led to better animal performance than the opposite scenario. This result was likely due to the animals exhibiting compensatory gain after being moved from a more restrictive to a less restrictive environment (Hornick et al., 2000; Peripolli et al., 2017). We did not observe important differences between the additive genetic variances in response to pasture and feedlot environments. However, the genetic covariances between these terms and the intercept were divergent (opposite signs). Animals with a high intercept (high overall performance level) for W378 tended to show increased genetic merit in better feedlot environments and decreased merit in more favorable pasture environments, and vice versa. Therefore, a moderate genetic antagonism in responses to pasture and feedlot environments appears to exist. Some degree of bias due to compensatory growth cannot be ruled out. Incorporating weaning weight into the analyses may help mitigate this effect and warrants further investigation; however, it would add complexity to the model. More complex models require larger datasets for proper convergence of the analyses.

To date, genetic responses of beef cattle for the same trait in both pasture and feedlot environments do not appear to have been reported in the literature for further comparisons. In dairy cattle, the intercept of reaction norms has been reported to correlate negatively (unfavorably) with the genetic response of animals to environmental challenges such as heat stress (Carabaño et al., 2019; Shi et al., 2021). In our study, pasture environments can be considered more challenging than feedlot environments. This similarity in genetic

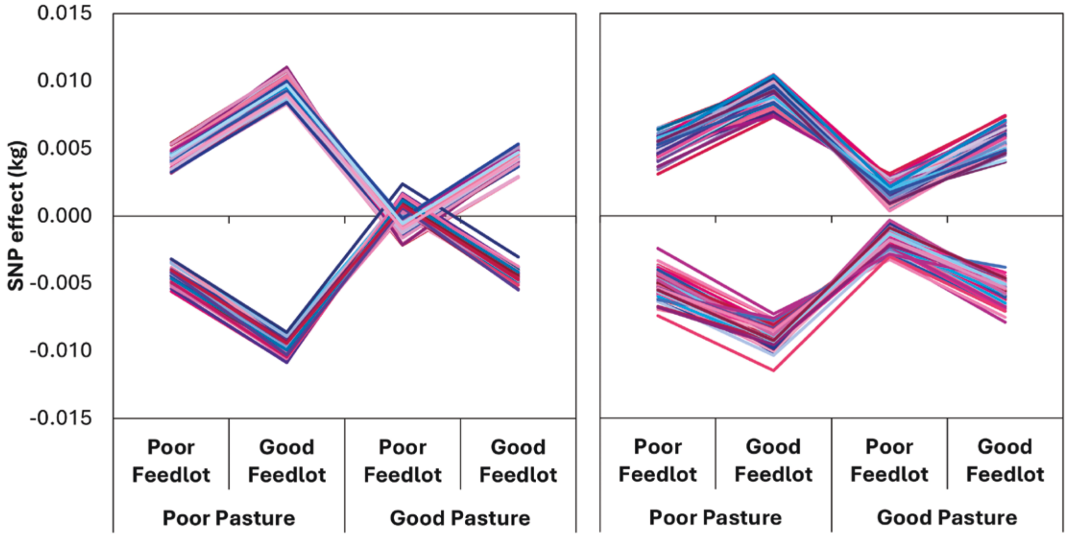

Figure 6. Posterior means of the SNP effects for body weight at approximately 378 d of age of Nellore cattle across different combinations of pasture and feedlot environments. The left panel shows a sample of the top 1% SNPs shared only between the genetic responses to the environments and not the intercept of the reaction norms. The right panel presents the top 1% SNPs associated exclusively with the intercept and not with the genetic responses to the environments.

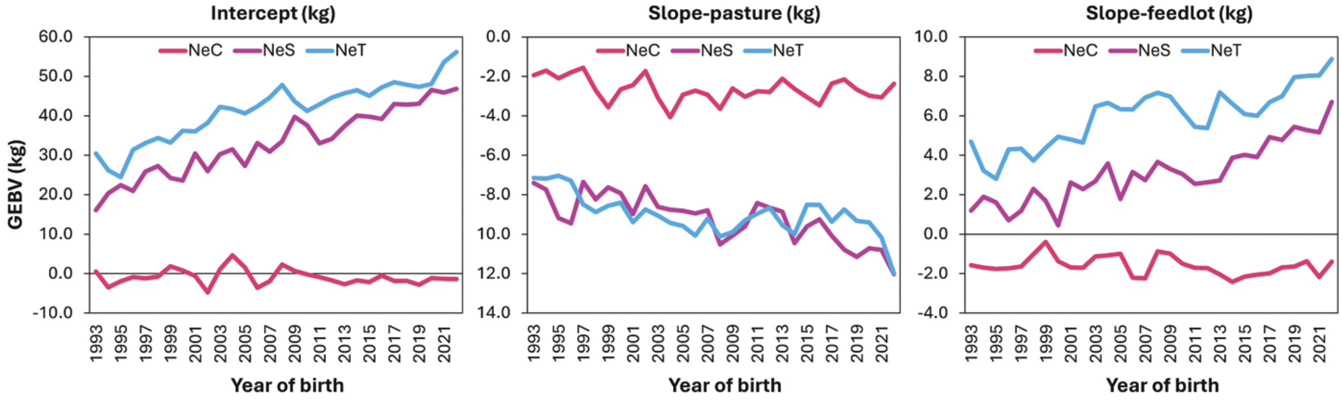

Figure 7. Posterior means of genomic estimated breeding values (GEBV) for the intercept and slopes for pasture and feedlot environments of the body weight at approximately 378 d of age of Nellore cattle according to the selection line (Nellore Control—NeC, Nellore Selection—NeS, and Nellore Traditional—NeT) and year of birth.

Table 3. Genomic windows that explained more than 1% of the total additive genetic variance (Var) for response to pasture environment of body weight at around 378 d of age in Nellore cattle and the corresponding list of annotated genes and traits previously associated

BTA	Var (%)	Start (bp)	End (bp)	Gene symbol[1]	Traits previously associated[2]	
					Beef cattle	Dairy cattle
7	2.318	106,890,739	107,300,339	*FBXL17*	Shear force	Digital cushion thickness, Milk yield and quality, Sole hemorrhage
29	1.523	1,712,507	2,122,107	*SLC36A4*, *MTNR1B*, *FAT3*	—	—
4	1.346	33,435,697	33,845,297	*ELAPOR2*, *GRM3*	Hip width, Marbling score	Calving ease, Pregnancy, Laminitis, Productive life, Milk yield and quality, Stillbirth, Strength, Udder conformation
11	1.344	72,613,994	73,023,594	*MAPRE3*, *SNORA62*, *DPYSL5*, *CENPA*, *SLC35F6*, *KCNK3*, *CIB4*, *CIMIP2C*, *OTOF*,	—	—
7	1.126	110,096,920	110,506,520	*CAMK4*	—	—

[1] All genes with start and end positions fully or partially overlapping with the relevant genomic windows are reported.
[2] Results based on the Animal QTLdb database.
BTA = *Bos taurus* autosome.

responses between dairy and beef cattle might be a coincidence of results or could relate to a more complex adaptive issue, as described by Taylor and Gabriel (1992) , Beckerman et al. (2010), and Carter et al. (2017). Those authors demonstrated how prey species might shape their growth according to the challenge faced. In situations of small size-selective predation, waterfleas (*Daphnia pulex*) exhibited delayed maturation at a larger size, representing investment in growth over reproduction. In contrast, with large size-selective predation, waterfleas showed accelerated maturation at a smaller size, indicating investment in reproduction over growth. Regardless of the underlying mechanisms for antagonistic genetic responses of beef cattle in pasture and feedlot environments, environmental sensitivity (also called phenotypic plasticity) can facilitate the maintenance of genetic variation in populations inhabiting heterogeneous environments (Carter et al., 2017).

An expressive magnitude of G × E effect for pasture and feedlot environments was observed, as described by the ratio of slope to intercept in the reaction norms. It is important to note that the population studied here represents a relatively limited range of environments, as it consists of a single population maintained in the same location. However, there was substantial variation in environmental conditions throughout

Table 4. Genomic windows that explained more than 1% of the total additive genetic variance (Var) for response to feedlot environment of body weight at around 378 d of age in Nellore cattle and the corresponding list of annotated genes and traits previously associated

BTA	Var (%)	Start (bp)	End (bp)	Gene symbol[1]	Traits previously associated[2]	
					Beef cattle	Dairy cattle
10	11.398	88,584,572	88,994,172	*TMED8, SAMD15, NOXRED1, VIPAS39, AHSA1, SPTLC2, ALKBH1, SLIRP, SNW1, U6, ADCK1*	—	—
18	4.142	54,611,397	55,020,997	*BICRA, EHD2, NOP53, SNORD23, CRX, ELSPBP1, CABP5, LIG1, ZSWIM9, ZNF114, ODAD1*	—	—
5	3.058	114,131,218	114,540,818	*MPPED1, EFCAB6, SULT4A1*	Body weight, intramuscular fat, monounsaturated fatty acid content	Heat tolerance, milk yield and quality
7	2.858	15,009,325	15,418,925	*KEAP1, S1PR5, ATG4D, KRI1, CDKN2D, AP1M2, SLC44A2, ILF3, QTRT1, DNM2, MIR199A1, TMED1, C7H19orf38, CARM1, YIPF2, TIMM29*	Bovine respiratory disease susceptibility, intramuscular fat, body weight	Calving ease, pregnancy, milk yield and quality, milkability, body conformation, productive life, somatic cell score, Stillbirth, udder and teat conformation
3	2.237	87,605,069	88,014,669	—	—	Milk yield and quality
4	1.591	91,571,401	91,981,001	*ZNF800, GCC1, ARF5, FSCN3, PAX4, SND1*	—	Calving ease, pregnancy, gestation length, milk yield and quality, milkability, body conformation, productive life, stillbirth, udder and teat conformation
7	1.498	16,165,332	16,574,932	*INSR, ARHGEF18, PEX11G, TEX45, ZNF358, MCOLN1, PNPLA6, CAMSAP3, XAB2, PET100, PCP2, STXBP2, RETN, MCEMP1, TRAPPC5, FCER2, CLEC4G*	Fat area to ribeye area ratio, hip width, hip width, body weight, body weight gain	Calving ease, pregnancy, milk yield and quality, milkability, body conformation, productive life, somatic cell score, stillbirth, udder and teat conformation
6	1.251	26,258,799	26,668,399	*RAP1GDS1, U6, STPG2*	Interval to first estrus after calving, body weight, marbling score, tenderness score, connective tissue amount	—
15	1.063	36,964,576	37,374,176	*INSC*	—	—
4	1.013	92,722,156	93,131,756	*CALU, OPN1SW, CCDC136, FLNC, MIR2422, ATP6V1F, SPMIP1, KCP, IRF5, TNPO3, MIR1843, TSPAN33, SMO*	Connective tissue amount	—

[1] All genes with start and end positions fully or partially overlapping with the relevant genomic windows are reported.
[2] Results based on the Animal QTLdb database.
BTA = *Bos taurus* autosome.

each year and across more than 40 yr with phenotypic records. The magnitudes of G × E observed in this study were like those reported by Pegolo et al. (2011) for weights at 210, 365, and 450 d of age in Nellore cattle raised in over 300 herds across different regions of Brazil (0.21 to 0.28). The degree of G × E indicated by the ratio of variance in the reaction norm is a key parameter for determining optimal selection environments (Kolmodin and Bijma, 2004). Similarly, the estimates of heritability in different environments directly affect selection responses. The results obtained here revealed variation in heritability estimates across different levels of environmental descriptors, reflecting substantial heterogeneity in variance across environments. These findings suggest potential divergences in the responses to selection for W378 depending on the production environment considered (pasture vs. feedlot). Previous studies have reported heterogeneity in variances and heritability estimates in different production environments for Nellore cattle (Pegolo et al., 2011; Ribeiro et al., 2015; Carvalho Filho et al., 2022) and between pasture and feedlot environments (Raidan et al., 2015).

In general, genetic correlations for W378 between different combinations of pasture and feedlot environments were high. However, estimates of genetic correlation between divergent environments were observed to differ from unity. Thus, selection for W378 in certain pasture environments may not be as effective as anticipated for achieving optimal responses in feedlot environments, and vice versa. Johnston et al. (2003) estimated genetic correlations ranging from 0.85 to 0.99 for body weight of temperate and tropical breeds between finishing regimes of pasture and feedlot. Raidan et al. (2015) found genetic correlations between pasture and feedlot of 0.75 for final weight and 0.49 for average daily gain in Nellore cattle subjected to performance tests. These authors highlighted that selection intensity is a critical parameter when dealing with G × E in pasture and feedlot environments. In this regard, Raidan et al. (2015) demonstrated that when there is no difference in selection intensity applied to selection candidates, feedlot production is the more efficient environment for achieving responses under feedlot conditions. Conversely, similar indirect responses to those obtained under feedlot can be achieved when the selection intensity applied to candidates evaluated on pasture is greater than the intensity applied to candidates evaluated in feedlot.

Reaction norms for sires and SNP reinforced the existence of G × E for W378 between different levels of pasture and feedlot environments. Similar results were obtained by Carvalheiro et al. (2019) for postweaning weight gain and Carvalho Filho et al. (2022) for yearling weight in Nellore cattle. We identified top SNP exclusively associated with the intercept or with the slopes of the reaction norms. Alternatively, selection to enhance responses to different pasture and feedlot environments without affecting the general performance level could be achieved through selection indices and eigen-decomposition of the covariance matrix of the random regression coefficients (Lin and Togashi, 2005; Carabaño et al., 2014; Macciotta et al., 2017).

Genetic trends revealed a significant increase in the general performance level, as assessed by the intercept of the reaction norms, for animals from the selected lines compared to the control line. It was observed that the response to pasture environments has been gradually reduced over the years for the selected lines. Conversely, the response to feedlot environments has increased for these lines. Indeed, the selection practiced in the current population has focused on male performance at the end of the performance test, i.e., under feedlot conditions. Thus, we expected to observe more pronounced and favorable genetic changes for this specific genetic component. These results also confirm the existence of genetic antagonism in the animals' responses to pasture and feedlot environments. The ongoing evolution of this scenario may have significant implications for the future selection of the current population and other herds. The herd analyzed here has a well-established genetic breeding program and provides genetic resources to various herds throughout Brazil, particularly those based on pasture systems. Selection practices have been previously identified as factors affecting the environmental sensitivity of various traits in this Nellore population (Freitas et al., 2021; Silva Neto et al., 2024).

Regarding the GWAS conducted for the response terms, we found that the slope of the reaction norms for pasture exhibited a more evident polygenic nature compared to the slope for feedlots. In other words, a greater number of genomic regions located across the genome had small contributions to the total additive genetic variance of the slope for pasture compared to the slope for feedlot. Therefore, the genetic architecture of the response to pasture environments appears to be more complex. Pasture environments are often more challenging and typically exhibit greater variability across years compared to feedlot conditions. This increased variability may induce a broader range of physiological and physical response mechanisms in the animals, potentially contributing to the greater genetic complexity observed in responses to pasture environments.

Among all the genomic windows that explained at least 1% of the total additive genetic variance, none overlapped between the genetic response terms for pasture and feedlot conditions for W378. Thus, the genetic antagonism between responses to different environments poses a significant challenge to optimizing the genetic responses of animals in both pasture and feedlot conditions.

Several genes were identified around the top genomic windows, which have been previously associated with important traits in beef cattle populations. Moreover, the genomic regions reported here were linked to biological processes and molecular functions crucial for animal performance. For the pasture slope, we highlight some identified genes such as *FBXL17* (*F-Box and leucine-rich repeat protein 17*) located on BTA7. This gene is expressed at different levels in the skeletal muscle of cattle from 6 to 12 mo old (Sadkowski et al., 2006). Furthermore, *FBXL17* has been previously associated with visual conformation score in Nellore cattle (Carreño et al., 2019), stayability in Nellore cattle (Silva et al., 2024), and chest depth in Qinchuan cattle (Yu et al., 2023). The *MTNR1B* (*Melatonin receptor 1B*) gene located on BTA29 was linked to resistance to tropical theileriosis in a Portuguese autochthonous breed (*Bos taurus taurus*) (Valente et al., 2024) and female reproductive success in *Bos taurus indicus* × *Bos taurus taurus* composites (McDaneld et al., 2014). The *KCNK3* gene located on BTA11 has been described as involved in potassium–sodium pumps in tender meat (Bongiorni et al., 2016). The *OTOF* gene was highlighted as a candidate gene for milk yield in Guzerat cattle (*Bos taurus indicus*) (Paiva et al., 2020), while the *DPYSL5* gene was found close to a SNP associated with growth traits in Charolais beef cattle (Jahuey-Martínez et al., 2016).

For the feedlot slope, we identified the genes *TMED8*, *SAMD15*, *NOXRED1*, *VIPAS39*, *AHSA1*, *SPTLC2*, *ALKBH1*, *SNW1*, and *ADCK1* on BTA10, which have been previously associated with respiratory issues such as lung consolidation and bovine respiratory disease in Holstein cattle (Quick et al., 2020). Bovine respiratory disease is recognized as a major health problem for feedlot cattle (Baptista et al., 2017). The *EHD2* gene located on BTA18 has one of the single SNPs explaining the largest proportion of the total additive genetic variance for ribeye muscle area in Nellore cattle (Tizioto et al., 2013). Murata et al. (2021) found that the *KEAP1* gene located on BTA7 was involved in a pathway providing a protective role in bovine endometrial epithelial cells under heat stress conditions. The *ZNF800* gene located on BTA4, which primarily acts in cell growth control, was associated with the essential fatty acid content of intramuscular *longissimus thoracis* in Nellore cattle (Schettini et al., 2022). A large number of genes in the genomic regions of BTA4 (*GCC1*, *ARF5*, *FSCN3*, *PAX4*, *SND1*, *CALU*, *OPN1SW*, *CCDC136*, *FLNC*, *MIR2422*, *ATP6V1F*, *KCP*, *IRF5*, *TNPO3*, *MIR1843*) as well as *PEX11G*, *TEX45*, *ZNF358*, *MCOLN1*, and *PNPLA6* located on BTA7 explained more than 1% of the total additive genetic variance for heifer early calving at different ages in Nellore cattle (Mota et al., 2022). On BTA7, the *CLEC4G* gene was expressed more in tender meat of Nellore cattle (Fonseca et al., 2017). Variations in the *SMO* gene on BTA4 can affect body size traits in Qinchuan beef cattle (*Bos taurus*) (Zhang et al., 2015). In a study on efficiency-related traits in Nellore cattle, which included part of the population analyzed here, Mota et al. (2022) found that genes identified on BTA7 have significant effects on muscle (e.g., *ARHGEF18*) and energy metabolism (*INSR*, *RETN*). The *ARHGEF18* gene influences energy expenditure in skeletal muscle necessary for maintenance, thereby enhancing feed efficiency by reducing oxidative stress (Mota et al., 2022).

The future implementation of the “double” reaction norm model in routine genetic evaluation in Brazil depends on integrating this methodology into national breeding programs. This approach would allow for an assessment of genotype-by-environment interactions, optimizing selection for animals better suited to both pasture and feedlot conditions. Key steps include validating the model using extensive performance and genomic data, developing computational strategies for large-scale implementation, and collaborations with breeding associations to refine selection indices. In addition, having user-friendly computer application tools to facilitate the visualization and comparisons of breeding values for different environments would be of great value.

Conclusions

The use of a “double” reaction norm model revealed divergent genetic responses of W378 of the same animals across pasture and feedlot environments. Due to a moderate genetic antagonism, the selected lines for increasing yearling weight of the studied Nellore population have gradually shown better performance in more favorable feedlot conditions at the expense of poorer performance in optimal pasture conditions. Therefore, the G × E between pasture and feedlot environmental gradients should be considered by breeding programs aiming to provide genetic material for environments different from those in which selection is performed. The genetic response of animals to pasture environments exhibited a more evident polygenic nature compared to the response to feedlot conditions, making selection in pasture environments a more complex task. Important genomic regions explaining a substantial portion of the genetic variation in responses to both pasture and feedlot environments were identified. These regions may be further explored to optimize the performance of beef cattle in various production environments.

Supplementary Data

Supplementary data are available at *Journal of Animal Science* online.

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Conflict of interest statement. The authors declare no real or perceived conflicts of interest.

Author contributions

Mário L. Santana (Conceptualization, Formal analysis, Investigation, Methodology, Software, Writing—original draft, Writing—review & editing), Annaiza B. Bignardi (Methodology, Resources, Validation, Visualization, Writing—review & editing), Gustavo R. D. Rodrigues (Methodology, Validation, Visualization, Writing—review & editing), Joslaine N. S. G. Cyrillo (Data curation, Resources, Writing—review & editing), Luiz F. Brito (Investigation, Validation, Writing—original draft, Writing—review & editing), and Maria E. Z. Eugenia Mercadante (Data curation, Resources, Writing—review & editing)

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