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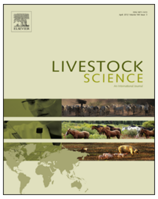

Genome-wide association study of temperament and tenderness using different Bayesian approaches in a Nellore–Angus crossbred population

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ABSTRACT

Genomic prediction models using Bayesian inference determine marker associations based on available data. The objective of this study was to evaluate marker associations for two traits using different Bayesian models applied to a crossbred population. Nellore–Angus F_2, F_3 and half-sibling calves were used with records for overall temperament at weaning (TEMP; a subjective scoring system on a 1–9 scale, where 1 is docile or calm and 9 is wild or unruly; $n=769$) and Warner–Bratzler shear force (WBSF; a measure of tenderness; $n=387$). After quality control filtering, there were 34,913 SNP markers distributed across the genome available for use (excluding the Y chromosome). An unknown proportion of these markers (designated as π) were assumed not to contribute to the variation in these traits. Bayesian methods employed were BayesC to estimate the ideal π (i.e., value that used as few markers as possible while maintaining heritability, designated as $\tilde{\pi}$). For WBSF or TEMP, $\tilde{\pi}=0.995$ or 0.997, respectively. Then BayesB (using $\tilde{\pi}$) or BayesC (using $\pi=0$ or $\tilde{\pi}$) were fitted to estimate SNP marker effects. Markers were mapped to genes closest to their placement on *Bos taurus* UMD 3.1 assembly and grouped into 1 Mb windows to identify associated regions, where association was determined based on the posterior probability of association of that window being greater than 0.75. No regions associated with either trait were found using $\tilde{\pi}$, but with $\pi=0$, 37 and 147 regions were found to account for more variation than expected under an infinitesimal model for TEMP and WBSF, respectively. Genes from windows identified as associated were used to conduct enrichment analyses. Significant ontology terms related to sodium ion transport and activity, especially voltage-gated channel activity were identified for TEMP, which could be identifying genetic differences between nervous system response to environment and stress stimuli in this population. For WBSF, significant ontology terms related to activity of serine peptidases were identified, but little is known about their true role in muscle tenderness, although they are known to be expressed in muscle.

1. Introduction

The concept of using genome-wide markers to find associations with quantitative trait loci (QTL) by Bayesian methods was introduced in the mid-1990s (Satagopan and Yandell, 1996; Satagopan et al., 1996; Sillanpää and

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Arjas, 1998; Stephens and Fisch, 1998). The Bayesian framework provided by Meuwissen et al. (2001) was the first to extend QTL mapping theory on a genome-wide scale to prediction of breeding values (i.e., genetic merit). Bayesian approaches are flexible in accounting for uncertainties in the data and allow for inferences to be made by averaging across all possible models rather than selecting a single model, thereby providing more robust inferences than non-Bayesian methods (Gianola et al., 2003; Meuwissen et al., 2001; Xu, 2003; Yi and Shriner, 2008). Traditional, non-Bayesian genome-wide association methods have been useful in detecting marker associations, but often only account for a small overall proportion of the genetic variance and most methods are usually hindered when the number of markers or segments is greater than the number of observations (reviewed by Fernando and Garrick, 2013).

Much research since Meuwissen et al. (2001) has focused on application of Bayesian methods for genomic predictions, with studies more recently reporting associations using Bayesian methods (e.g., Boddicker et al., 2012; Onteru et al., 2011, 2012; Veerkamp et al., 2010). Limited simulated studies (e.g., Calus et al., 2009; Veerkamp et al., 2010) discussed differences between methods or their impacts on the differing goals of QTL mapping versus prediction of genetic merit using Bayesian inference, although some studies using real data have compared Bayesian methods for prediction of genetic merit (e.g., Habier et al., 2011). Furthermore, association studies for traits like muscle tenderness measured using Warner–Bratzler shear force as well as temperament (either subjective or quantitative) have used traditional as well as genome-wide association methods to find associated genomic regions (e.g., Casas et al., 2001, 2003; Gutiérrez-Gil et al., 2008a), but limited studies have utilized Bayesian methods for association analyses (e.g., Snelling et al., 2013).

The objectives of this study, therefore, were to (1) compare association results using BayesB and BayesC (with $\pi=0$ or an estimation of π) using a Nellore–Angus crossbred population; and (2) to identify significant ontology terms using genes identified in those associated regions for overall temperament at weaning (TEMP) and Warner–Bratzler shear force (WBSF).

2. Materials and methods

2.1. Cattle

A Nellore–Angus crossbred population located at the Texas A&M AgriLife McGregor Research Center was used in this study. Cycle 1 of this population consisted of 13 full-sibling F_2 families and 4 paternal half-sibling families (Table 1). The F_2 families were founded by Nellore (N) grandsires and Angus (A) granddams. Four NA F_1 sires were mated to 13 NA F_1 dams to produce 13 full-sibling families by multiple ovulation and embryo transfer (ET). The 4 NA F_1 sires were also mated to an additional population of F_1 and F_2 *Bos indicus* (Brahman or N) × *Bos taurus* (Hereford or A) cows to produce paternal half-sibling families through natural service. These calves were produced in multiple-sire pastures so DNA testing was used to determine paternity. A total of 480 NA × NA F_2 ET and 266 natural service calves were produced from 2003 to 2007. There were 10 NA × NA F_2 ET bull calves retained to produce another generation of the population and these bulls were excluded from phenotypic analyses.

Table 1
Cattle population structure and number of progeny used in the study.

Cycle	Family[b]	Type of cross[c]	Number of progeny[a]		
			Born	Used (TEMP)	Used (WBSF)
1	70	F_1 NA × F_1 NA	36	33	17
	71	F_1 NA × F_1 NA	70	63	26
	72	F_1 NA × F_1 NA	46	45	22
	73	F_1 NA × F_1 NA	10	7	5
	74	F_1 NA × F_1 NA	8	8	4
	75	F_1 NA × F_1 NA	44	36	14
	76	F_1 NA × F_1 NA	10	7	5
	77	F_1 NA × F_1 NA	42	41	23
	80	F_1 NA × F_1 NA	70	66	30
	81	F_1 NA × F_1 NA	64	56	33
	82	F_1 NA × F_1 NA	16	15	7
	83	F_1 NA × F_1 NA	38	36	15
	84	F_1 NA × F_1 NA	30	28	12
	95	F_1 NA × Cross	70	68	30
	96	F_1 NA × Cross	123	119	38
	97	F_1 NA × Cross	56	56	30
	98	F_1 NA × Cross	17	15	7
2	2102	F_1 NA × F_1 NA	22	10	10
	2227	F_1 AN × F_1 NA	18	7	7
	2229	F_1 AN × F_1 NA	3	1	1
	2230	F_1 AN × F_1 NA	5	2	2
3	3150	F_2 NA × F_2 NA	6	4	4
	3151	F_2 NA × F_2 NA	6	3	3
	3152	F_2 NA × F_2 NA	10	2	2
	3153	F_2 NA × F_2 NA	7	3	3
	3154	F_2 NA × F_2 NA	4	1	1
	3155	F_2 NA × F_2 NA	26	18	17
	3156	F_2 NA × F_2 NA	23	8	8
	3157	F_2 NA × F_2 NA	9	5	5
	3159	F_2 NA × F_2 NA	11	6	6
			Total:	769	387

[a] Progeny born in a particular family may have died or been sold prior to collection of the respective trait, where TEMP = overall temperament at weaning and WBSF = Warner–Bratzler shear force.

[b] Family is referencing a mating of animals that includes either full-sibling or half-sibling progeny.

[c] NA is Nellore (N) × Angus (A) cross, where sire breed is listed first. "Cross" could be an F_1 or F_2 *Bos indicus* (Brahman or N) × *Bos taurus* (Hereford or A).

Cycles 2 and 3 of this population were a continuation of crosses using N and A breeds (Table 1). The Cycle 2 population consisted of all possible combinations of reciprocal natural service F_2 calves (NA × NA, NA × AN, AN × AN, and AN × NA crosses of F_1 cattle) produced from 2009 to 2011, but only steers from a subset of these crosses (NA × NA and AN × NA) were available for this study. The Cycle 3 population of NA × NA F_3 calves was produced by natural service at the same time as the Cycle 2 calves. To minimize inbreeding, NA × NA F_2 ET bulls by two of the F_1 sires were bred to F_2 ET females by the other two F_1 sires, and vice versa. There were 169 calves of the Cycle 2 and 3 matings produced from 2009 to 2011 with records available but only the steers ($n=70$) were genotyped for this