Association of Polymorphisms in the IGF1, GH and PIT1 Genes with Growth and Reproductive Traits in Canchim Cattle

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Introduction

A variance component approach for quantitative trait loci (QTL) mapping was proposed by George *et al*. (2000), which assumes a mixed inheritance model (polygenes and QTL effects). This approach allows for mapping QTL in general pedigrees from outbreed populations. In this method, besides the use of an additive relationship matrix to estimate the additive polygenic effects, an identical-by-descent (IBD) matrix is used to estimate the QTL effect and its variance. Analyses of the association of genetic markers with economic traits in beef cattle have been mainly reported in developed countries. In the Brazilian Canchim breed, studies found association of polymorphism in the insulin-like growth factor 1 (IGF1), growth hormone (GH) and specific pituitary transcriptions (PIT1) genes with growth traits (Pereira *et al*. (2005), Andrade *et al*. (2008) and Carrijo *et al*. (2008)). However, no studies were found that used the variance component approach to estimate the genetic variance due to these genes, or QTLs linked to them, in Canchim cattle.

The objective of this study was to estimate the proportion of phenotypic variance of growth and reproductive traits that are explained by polymorphisms in the IGF1, GH and PIT1 genes in Canchim cattle.

Material and methods

The animals used in this study were from a breeding program carried out at Embrapa Pecuária Sudeste, São Carlos, state of São Paulo, Brazil, for the development of the Canchim synthetic breed. This herd is managed in pastures and records of growth and reproductive performance are taken routinely. For the statistical analyses, the animals were classified in 12 genetic groups (GG), considering the genetic composition of animal and its parents. The contemporary groups (CG) were defined as animals from the same GG and born in the same year and breeding season (spring, summer, fall and winter).

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The genotype data were provided by Embrapa Pecuária Sudeste. The number of animals with genotypes for one microsatellite in the IGF1 gene (four alleles) and one single nucleotide polymorphism in the GH and PIT1 genes were 1397, 755 and 517, respectively. The methods for DNA extraction, amplification, and polymorphism identification in IGF1 and GH genes are described in Regitano (1999) and Andrade *et al*. (2008) and in the PIT1 gene they are described in Carrijo *et al*. (2008).

Statistical analyses: The traits analyzed included: birth weight (BW), weaning weight (WW), average daily gain from birth to weaning (ADG), body weight at 12 (W12) and at 18 months (W18), age at first calving (AFC), body weight at first calving (WFC), scrotal circumference at 12 (SC12) and at 18 months of age (SC18).

The analyses were performed in two steps, using Loki release 2.4.6 (Health (1997)) to estimate the IBD matrices and using ASREML release 3.0 (Gilmour *et al*. (2009)) to fit the linear model.

Phenotypic records were first adjusted for all known environmental effects, i.e. the random effect of CG for all traits, and the fixed effects of age of dam (linear and quadratic covariate) and sex for BW; age of dam (linear and quadratic covariate), sex and age at weaning (linear covariate) for WW and ADG; sex and age at measurement (linear covariate) for W12 and W18; age of dam (linear and quadratic covariate) for AFC; age at measurement (linear covariate) and W12 (linear covariate) for SC12; age at measurement (linear covariate) and W18 (linear covariate) for SC18. For WFC only CG effect was fit.

After adjusting the records for environmental effects, they were analyzed with two different animal models, using ASREML. The full model (polygenes + QTL) assumes that the genetic contribution to the trait is due to the polymorphism in the gene under examination (IGF1, GH or PIT1) plus an unlinked polygenic effect. The reduced model (polygenes only) assumes that the genetic contribution is only due to polygenic effects. The (co)variance matrices for polygenic and QTL effects were assumed proportional to the additive relationship matrix and to the IBD matrix, respectively.

The significance of the QTL effects was tested by likelihood ratio test, comparing the maximum likelihood of the full and reduced models.

Results and discussion

The number of animals analyzed and the estimated heritabilities for full and reduced models for BW, WW, ADG, W12, W18, AFC, and WFC are shown in Table 1. All heritabilities, except for SC12 and SC18, were lower compared to the estimates reported in other studies in Canchim cattle (e.g., Silva *et al*. (2000); Talhari *et al*. (2003) and Mucari *et al*. (2007)). This might be a consequence of the small number of animals with records to estimate the heritability in the current study.

Table 1: Number of animals (N) and estimates of genetic parameters for full and reduced models for birth weight (BW), weaning weight (WW), average daily gain from birth to weaning (ADG), body weight at 12 months (W12), body weight at 18 months (W18), age at first calving (AFC), body weight at first calving (WFC), scrotal circumference at 12 months (SC12) and scrotal circumference at 18 months of age (SC18) in Canchim cattle.

Trait	IGF1				GH				PIT1			
	N	$h^2_{G_R}$	$h^2_{G_F}$	h^2_{QTL}	N	$h^2_{G_R}$	$h^2_{G_F}$	h^2_{QTL}	N	$h^2_{G_R}$	$h^2_{G_F}$	h^2_{QTL}
BW	1956	0.35	0.35	0.05	1287	0.33	0.32	0.00	926	0.24	0.24	0.03
WW	1893	0.29	0.29	0.00	1253	0.23	0.25	0.08	896	0.26	0.26	0.00
MDG	1893	0.26	0.26	0.00	1253	0.20	0.23	0.08	896	0.23	0.23	0.00
W12	1676	0.13	0.13	0.00	1134	0.17	0.18	0.04	841	0.16	0.16	0.00
W18	1462	0.14	0.14	0.00	1054	0.13	0.13	0.01	779	0.09	0.10	0.01
AFC	783	0.01	0.01	0.00	681	0.00	0.00	0.00	461	0.00	0.09	0.09
WFC	775	0.30	0.32	0.03	673	0.22	0.46	0.33	457	0.42	0.57	0.20
SC12	564	0.45	0.45	0.04	266	0.42	0.42	0.00	257	0.40	0.40	0.00
SC18	425	0.61	0.61	0.00	218	0.35	0.35	0.00	212	0.74	0.74	0.00

$h^2_{G_R}$ = reduced model heritability (polygenes); $h^2_{G_F}$ = full model heritability (polygenes+QTL); h^2_{QTL} = QTL heritability

The estimated portion of phenotypic variance attributed to the polymorphism in the IGF1, GH or PIT1 gene can be seen in Table 1 and the corresponding likelihood ratio tests with their respective significance levels are given in Table 2. Birth weight was significantly influenced by the polymorphism in the IGF1 gene, and WW and WFC were significantly influenced by the polymorphism in the GH gene. All other associations were not significant. The polymorphism in the IGF1 explained 5% of the estimated phenotypic variance, while the polymorphism in GH explained 8% and 33% of the estimated phenotypic variance for WW and WFC, respectively. The estimated value of 33% for WFC seems to be too high for a single polymorphism in the GH gene. This might be a consequence of the limited sample size for this trait.

An association between IGF1 and BW on the same herd was also reported by Andrade *et al*. (2008) and Pereira *et al*. (2005). These authors also did not find association of IGF1 with WW, W12 and W18. Regarding the polymorphism in the GH gene, Silveira *et al*. (2008) and Pereira *et al*. (2005) reported an association with WW and W12, respectively. The polymorphism in the PIT1 gene was not significantly associated with any of the traits considered. However, Carrijo *et al*. (2008), studying the same set of animals, but with another association analysis approach, found significant association between PIT1 and ADG.

Conclusion

The variance component analyses showed a significant association between a polymorphism in the IGF1 gene and birth weight in Canchim cattle, which explained 5% of the estimated phenotypic variance. In addition significant association of a polymorphism in the GH gene with weaning weight and weight at first calving was found, which explained 8 and 33% of the respective estimated phenotypic variances. These findings warrant further investigation

on the potential use of these polymorphisms as genetic markers for those three traits in Canchim cattle.

Table 2: Likelihood ratio test (LR) values for comparing the full model (polygenic + QTL effect) and the reduced model (polygenic effect only) for birth weight (BW), weaning weight (WW), average daily gain from birth to weaning (ADG), body weight at 12 months (W12), body weight at 18 months (W18), age at first calving (AFC), body weight at first calving (WFC), scrotal circumference at 12 months (SC12) and scrotal circumference at 18 months of age (SC18) in Canchim cattle.

Trait	LR_{IGF1}	LR_{GH}	LR_{PIT1}
BW	2.98*	0.00	0.52
WW	0.00	2.90*	0.00
MDG	0.00	0.00	0.00
W12	0.00	0.66	0.00
W18	0.00	0.06	0.02
AFC	0.00	0.00	0.08
WFC	0.14	5.84**	0.52
SC12	0.23	0.00	0.00
SC18	0.00	0.00	0.00

**P<0.01; *P<0.05; IGF1= insulin-like growth factor, GH=growth hormone, PIT1=specific pituitary transcription genes

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