Comparison of SNPs associated with residual feed intake during different fattening periods in Japanese Black cattle

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Summary

This study aimed to compare single nucleotide polymorphism (SNP) effects associated with residual feed intake (RFI) during the first half, latter half, and total fattening periods in Japanese Black cattle. Residual feed intake for each period was obtained from 4,578 Japanese Black steers, which were progeny of 362 sires. The Illumina BovineSNP50 v2 BeadChip was used for genotyping of all sires. The SNP effects were estimated using a single-step genome-wide association study (ssGWAS). The results indicated that the magnitude of genetic variance in SNP windows differed for each fattening period. In addition, a RNA gene involved in the post-transcriptional regulation of gene expression was located near a significant effect SNP window associated with RFI in the first half of the fattening period. These results would facilitate better understanding of the physiological mechanism regulating feed efficiency in beef cattle.

Keywords: ssGWAS, RFI, SNP effect, Japanese Black cattle

Introduction

Feed cost, especially of concentrated diets for feedlot cattle, is the main cost in Japanese beef production. Hence, there is an urgent need to improve the feed efficiency in feedlot cattle. Residual feed intake (RFI) is known as the net feed efficiency index (Koch *et al*., 1963). Few studies have estimated the genetic parameters for RFI in feedlot cattle; therefore, it remains unknown whether genetic influences for RFI differ between the fattening periods. In a genome-wide association study (GWAS), which is based on single marker regression, a single nucleotide polymorphism (SNP) effect is considered as a covariate and a phenotypic value as a dependent variable in the model. However, in cases where genotyped animals do not possess phenotypes but non-genotyped animals do possess phenotypes, the single-step GWAS (ssGWAS) has been proposed as an alternative method of analysis, because it aids the integration of all phenotypic and genotypic information in the pedigree for the estimation of SNP effects (Wang *et al*., 2012). This study aimed to compare genomic regions associated with RFIs during different fattening periods by ssGWAS. In the Japanese Black cattle population used for the study, there were genotyped sires without phenotypes as well as non-genotyped progenies with phenotypes.

Material and methods

Phenotypic and genotypic data

The phenotypic data (i.e., feed intake and body weight) were obtained from a total of 4,578 Japanese Black steers, which were progeny of 362 sires, that were performance tested at the stations of the Livestock Improvement Association of Japan Inc. (LIAJ) from 1998 to 2008. The pedigree information was traced back to five generations, and 30,012 animals were used in this study. Fattening of steers began at an average of 9.1 months of age and continued for up to 52 weeks thereafter. Residual feed intake was calculated for three periods of the fattening periods (first half, second half, and total fattening periods); RFIs for the first half of the fattening period (0–24 weeks), latter half of the fattening period (24–52 weeks), and total fattening period (0–52 weeks) were defined as RFI_E, RFI_L, and RFI_T, respectively.

The DNA samples of the 362 sires were genotyped using the Illumina BovineSNP50 v2 BeadsChip (Illumina, CA, USA) and GenomeStudio software (Illumina, CA, USA). After the SNP quality control, a total of 37,851 SNPs on autosomal chromosomes were available.

Singe-step genome-wide association study

Analysis by ssGWAS, as proposed by Wang *et al.,* (2012), was performed by using the following model:

$$\mathbf{y} = \mathbf{Xb} + \mathbf{Za} + \mathbf{e} \quad (1)$$

where **y** is the vector of observations; **X** and **Z** are the design matrices for fixed and random effects, respectively; **b** is the vector of fixed effects, including the contemporary group (year, step, station, and herd) and the beginning age of the test; and **a** and **e** are the vectors of random effects due to additive genetic effects, i.e., genomic estimated breeding value (GEBV) with $\mathbf{a} \sim N(0, \mathbf{H}\sigma_a^2)$ and residual effect with $\mathbf{e} \sim N(0, \mathbf{I}\sigma_e^2)$, respectively, where σ_a^2 and σ_e^2 are additive genetic and residual variances, respectively. **I** is an identity matrix, and **H** is a matrix that combines pedigree and genomic information. The inverse of **H** is calculated as follows:

$$\mathbf{H}^{-1} = \mathbf{A}^{-1} + \begin{bmatrix} \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{G}^{-1} - \mathbf{A}_{22}^{-1} \end{bmatrix} \quad (2)$$

where **A** is the numerator relationship matrix; $\mathbf{A_{22}}$ is the relationship matrix for genotyped animals; and **G** is the genomic relationship matrix. The estimation of SNP effects ($\hat{\mathbf{u}}$) was obtained using the following equation:

$$\hat{\mathbf{u}} = \lambda \mathbf{DW}'(\mathbf{WDW}')^{-1}\hat{\mathbf{a}}_g \quad (3)$$

where λ is a variance ratio; **W** is a matrix relating to genotypes of each locus; **D** is a diagonal

matrix of weights for variances of SNP (initially **D** = **I**); and $\hat{u}_g$ is the GEBV of genotyped animals. The procedure, which consists of a GEBV computation and the refinement of SNP weights through three iterations, was performed to estimate the SNP effect, as described by Wang *et al.* (2012). The proportion of genetic variance explained by the *i*-th region was calculated by a window of 20 adjacent SNPs. These analyses were performed by using the BLUPF90 family of programs (Misztal *et al.*, 2002). The characterized genes within ± 50 kb of the 20 consecutive SNPs, that explained more than 3.0% of the additive genetic variance, were scanned using the NCBI2R R package (http://cran.r-project.org/web/packages/NCBI2R/index.html).

Results and Discussion

Figure 1 shows Manhattan plots for each RFI by ssGWAS, indicating that the magnitude of each SNP effect was different depending on the fattening period. Table 1 shows DNA regions related to RFIs in three different fattening periods and the number of characterized genes located in the region. The highest SNP effects in RFI_E, RFI_L, and RFI_T were found on bovine chromosome (BTA) 12, 5, and 20, respectively. No region was commonly observed in all three RFI, nor in both RFI_E and RFI_L. However, three regions were commonly observed in RFI_E and RFI_T, and two regions were commonly observed in RFI_L and RFI_T. The region with the highest genetic variance explained for RFI_E of 61.7% was found on BTA 12. In this region only one microRNA, bta-mir-1256 (*MIR1256*) gene, which is involved in the post-transcriptional regulation of gene expression, was located. In addition, the same gene was detected in RFI_T. In a previous study on GWAS, the microRNA was associated with maternal calving difficulty (Purfield *et al*., 2013). On the other hand, RFI had a weak genetic correlation with maternal calving difficulty (Crowley *et al*., 2011). Hence, the existence of biological and genetic relationships between feed efficiency and calving difficulty can be presumed. The mitochondrial ribosome recycling factor (*MRRF*) gene, which is important for cell viability, was in the region of BTA11 associated with RFI_E and RFI_T. Some relationships between feed efficiency and mitochondrial function in livestock have been reported (Bottje & Carstens, 2008). Thus, further research is required to investigate the genetic effect of mitochondrial function on feed efficiency.

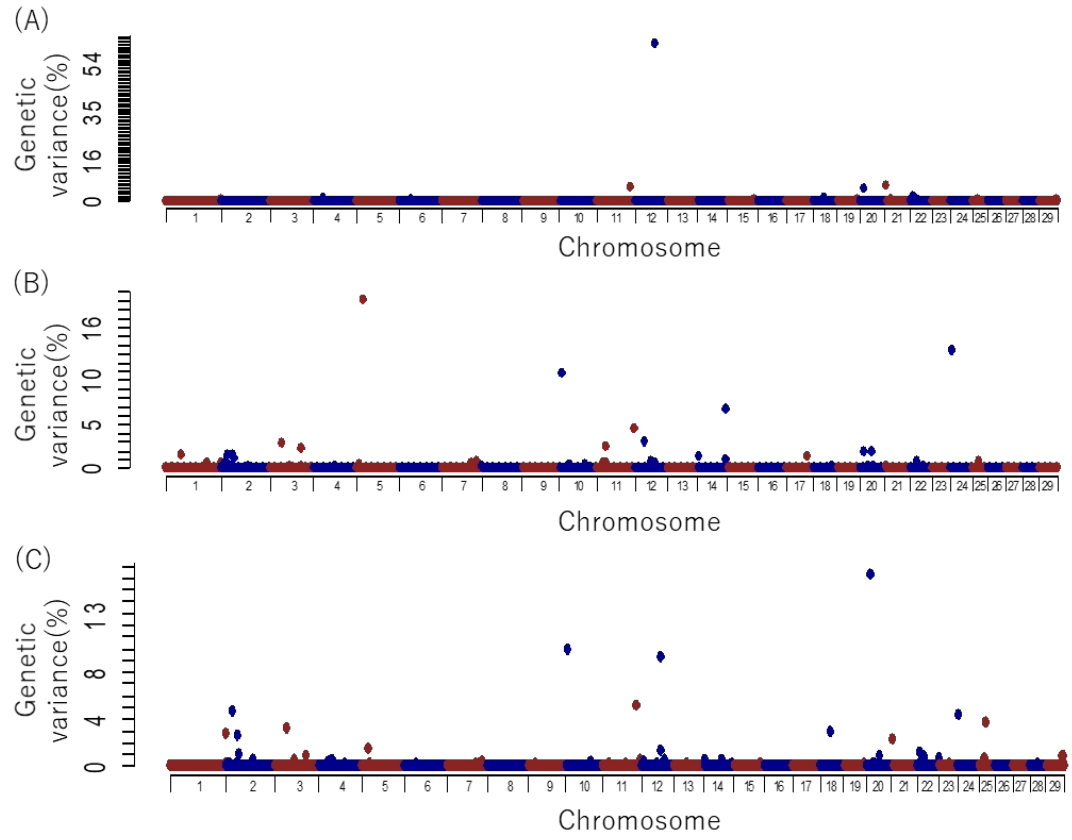

Figure 1. Manhattan plots for residual feed intake in the first half of the fattening period (A), latter half of the fattening period (B), and total fattening period (C).

Table 1. Genomic regions related to residual feed indices in the three different fattening periods and number of characterized genes located in each region.

Trait	Chromosome	Region (Mbp)	Number of characterized genes in the region	Proportion of genetic variance (%)
RFI_E	11	92.50–93.77	12	5.3
	12	56.95–57.80	1	61.7
	20	12.20–13.05	2	5.0
	21	0.04–3.25	6	6.1
RFI_L	5	16.33–19.02	5	19.1
	10	6.10–7.39	8	10.9
	11	103.06–104.09	25	4.6
	14	78.09–79.80	14	6.7
	24	1.58–2.35	0	13.3
RFI_T	2	15.92–17.14	2	4.7
	3	33.90–34.87	28	3.2
	10	6.10–7.39	8	9.9
	11	92.50–93.77	12	5.1
	12	56.95–57.80	1	9.3
	20	12.20–13.05	2	16.4
	24	1.58–2.35	0	4.3
	25	17.20–19.00	24	3.7

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