

Large-Scale SNP Association Analyses Of Residual Feed Intake And Its Component Traits In Pigs

D.M. Gorbach^{*}, W. Cai^{*}, J.C.M. Dekkers^{*}, J.M. Young^{*}, D.J. Garrick^{*}, R.L. Fernando^{*} and M.F. Rothschild^{*}

Introduction

The high genetic correlation between growth and feed intake has increased feed requirements as pigs have been selected for increased growth rate. The largest variable cost in swine production today is feed. Boggess *et al.* (2009) claimed that around \$500 million dollars annually could be saved by swine producers in the US by reducing the average feed:gain ratio from 2.75 to 2.45. Significant variability exists between pigs in the amount of feed intake required to achieve the same rate of growth. Residual feed intake (RFI) is a measure of the difference between what an animal actually consumes and the average amount of feed required for that animal's levels of maintenance and growth. It is believed that animals can be successfully selected for both increased growth and reduced RFI, to reduce the feed costs per-unit gain.

Iowa State University has selected pigs for decreased RFI over six generations. A single foundation population of Yorkshire pigs was divided into two lines by randomly splitting litters to form a select line for low RFI and a randomly selected control line (Cai *et al.* (2008)). Following five generations of random selection, the control line was subsequently selected for increased RFI. Phenotypic RFI was calculated by fitting a quadratic random regression equation as average daily feed intake (ADFI) = $(b_{1i} * \text{onTestWeight} + b_{2i} * \text{offTestWeight} + b_{3i} * \text{midTestWeight} + b_{4i} * (\text{average daily gain (ADG)} + b_{5i} * \text{offTestBackFat (BF)}))$, where the regression coefficients (b 's) were generation and line dependent. An animal model was used to estimate EBV from the phenotypic RFI observations (Cai *et al.* (2008)). Estimated heritability for RFI calculated in this manner was 0.29 and RFI explained 34% of phenotypic variation in ADFI (Cai *et al.* 2008). These results indicate that financial progress could be made by selecting for RFI, if this could be done using SNPs without the expense of collecting feed intake data.

Material and methods

Genotyping. Tail samples were collected from each animal at birth and used for DNA isolation. The Qiagen (Valencia, CA, USA) DNeasy blood & tissue kit was used for DNA isolation. A total of 730 animals were selected for genotyping from generations 0, 4, 5, and 6 of the Iowa State University RFI selection lines (Figure 1). Genotyped animals included, 716 with RFI data, with 329 control and 387 select animals. GeneSeek Inc. (Lincoln, NE, USA)

^{*} Iowa State University, 2255 Kildee Hall, Ames, IA 50011, USA

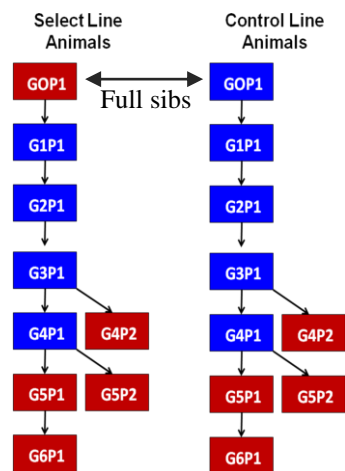


Figure 1: Generations and parities (P1/P2) of pigs in the ISU selection project with genotyped parities depicted in red.

effects. Fixed effects included line, sex, on-test group, pen fitted within group, and on-test age as a covariate, except for BF where on-test age was replaced with off-test weight. The prior probability that a SNP in \mathbf{Z} has zero effect was set to 0.995, corresponding to about 300 non-zero SNP effects fitted in any particular realization of the Monte-Carlo Markov Chain (MCMC) used for the Bayesian analysis. Following a 10,000 iteration burn-in period, 40,000 MCMC iterations were run. Results were obtained in the form of a post burn-in posterior distribution for the effect of every SNP fitted simultaneously with other informative SNPs. The posterior mean effect of each SNP across the chains was used to predict the genomic breeding value of every chromosomal fragment consisting of 5 contiguous loci (5-SNP overlapping windows). Each such window's contribution to the additive genetic variance in the population was then derived, a statistic that has a multi-locus analogy to $2pq\hat{a}^2$, the gene frequency specific contribution to genetic variance of the substitution effect of a single locus. That variance was divided by an estimate of the total genetic variance.

The most significant regions of the genome for RFI, ADFI, ADG, and BF were examined for genes based on build 9 of the porcine genome. Gene positions were taken from Ensembl (www.ensembl.org) identified by proximity to the most informative individual SNPs or 5-SNP windows and gene function.

Results and discussion

In Figure 2 SNP association results are shown for RFI, ADFI, ADG, and BF. Sets of 250-300 markers explained 33% of phenotypic variation for RFI. This number was close to estimated heritability (0.29 - Cai *et al.* (2008)) and litter variance of 4% (Bunter *et al.* (2010)). In the

completed the genotyping with the Illumina (San Diego, CA, USA) PorcineSNP60 BeadChip.

Phenotyping. Feed intake data was measured on all animals using electronic FIRE Feeders (Osborne, KS, USA) donated by PIC (Hendersonville, TN, USA), as described in Cai *et al.* (2008). Animals were weighed at least every two weeks to compute ADG. At approximately 115 kg, 10th-rib BF was evaluated with an Aloka ultrasound machine (Corometrics Medical Systems Inc., Wallingford, CT, USA).

Statistical analyses. Quality control included the removal of all single nucleotide polymorphisms (SNPs) which were fixed in the entire population or had a quality control (QC) score less than 0.4 in greater than 20% of the population. A total of 55,533 SNPs remained for analysis. Bayes C model averaging, as implemented in GenSel (<http://bigs.ansci.iastate.edu>) was used for data analyses. The regression model used was: $Y = \mathbf{X}\beta + \mathbf{Z}u + e$, where \mathbf{X} is an incidence matrix for fixed effects and \mathbf{Z} is a matrix of SNP genotypes fitted as random

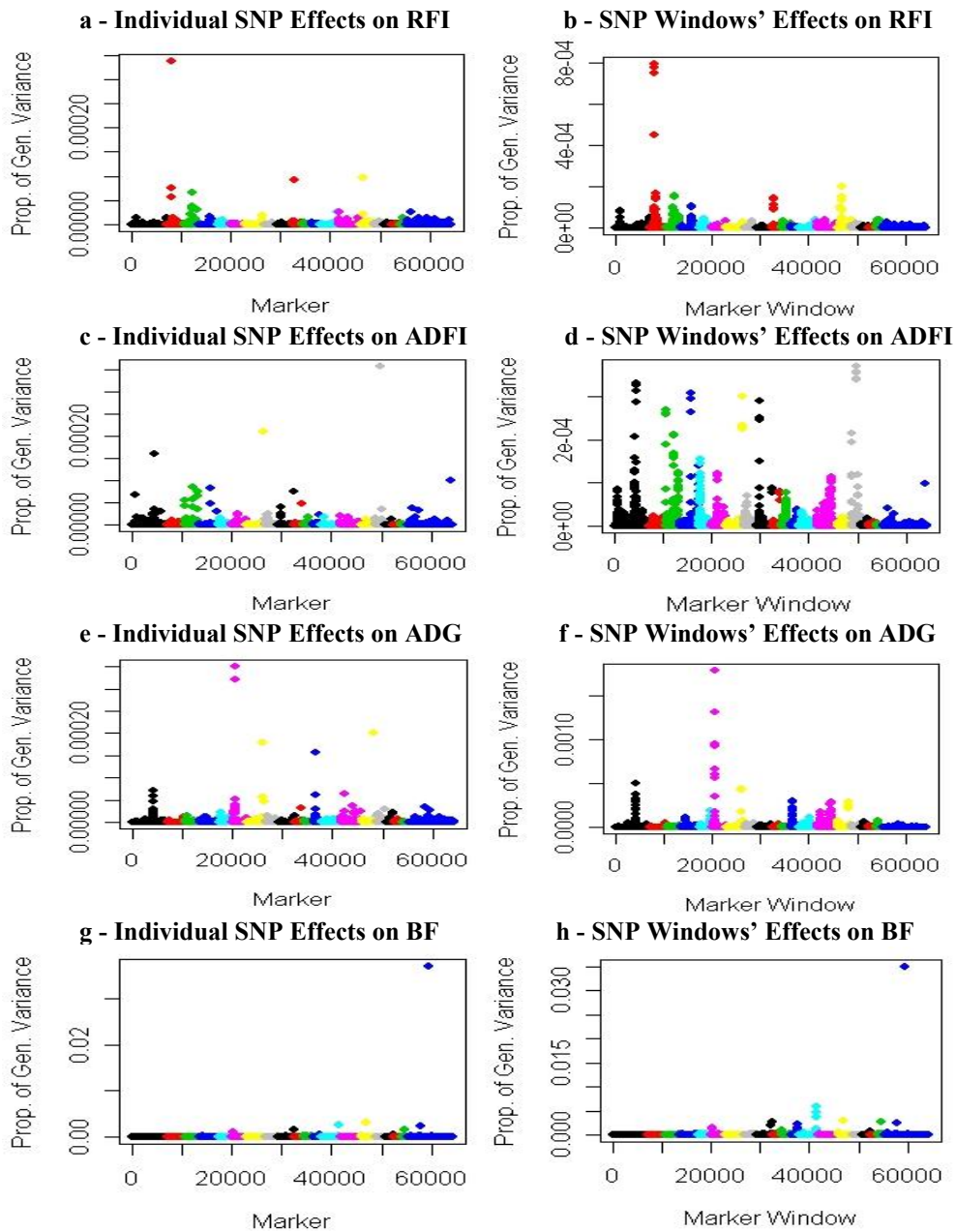


Figure 2: Proportion of genetic variance explained by each marker or window of 5 consecutive markers in the genome for each trait. Each chromosome is a different color with SSC1 on the left, SSC18 in red on the right, followed by SSCX in green and unmapped markers in blue. Note: y-axes differ in scale.

current study, litter was not fitted because few families had more than one genotyped offspring. For ADFI, ADG, and BF, 48%, 43%, and 69%, respectively, of the phenotypic variation was explained by sets of 250-300 markers. Heritabilities for these traits were estimated to be 0.51, 0.42, and 0.68, respectively, in this population (Cai *et al.* (2008)) and corresponded closely with the proportions of phenotypic variance explained by markers, as obtained from these marker analyses.

Proportions of genetic variance displayed in plots on the left side of Figure 2 reflect the genetic variance explained by single markers divided by the overall genetic variance of the trait explained by the sets of 250-300 markers. These values would be estimates of the true genetic variance accounted for by the SNP, if the SNP was in linkage equilibrium with the other SNPs. The existence of linkage disequilibrium (LD) reduces the genetic variance explained by each SNP as multiple SNPs share the effect of each QTL due to LD. Thus, SNP windows more accurately capture the contributions of QTL to genetic variance.

The largest SNP effect and largest SNP window effects for RFI were located on *S. scrofa* chromosome (SSC) 2 near 32 megabases (Mb) [coordinate position]. None of the other traits analyzed had large SNP effects in this region of SSC2. Some of the largest genetic effects for ADFI were near *MC4R* on SSC1 and around 49 Mb [coordinate position] on SSC16 near *FGF18*. Some of the largest effects for ADG were near 17 Mb [coordinate position] on SSC6 and near *MC4R* on SSC1. Finally, for BF, the largest effect was from an unmapped SNP that lacked high LD with any currently mapped SNPs. The largest effect on BF from mapped SNPs was around 143 Mb [coordinate position] on SSC13. The SNPs with large effects on RFI have potential to be used in marker-assisted selection (MAS) to reduce the feed intake requirements of pigs without negatively impacting other production traits. The economic impact of such a reduction would greatly benefit hog producers.

Conclusions

This study has identified SNPs that may be useful in marker-assisted selection to predict ADFI and/or RFI without the expense of gathering feed intake data in pigs. That information could be used in index selection approaches to simultaneously improve growth and reduce feed costs.

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