Large Effects on Birth Weight Follow Inheritance Pattern Consistent with Gametic Imprinting and X Chromosome.

R.M. Thallman[*], J.A. Dillon[†], J.O. Sanders[‡], A.D. Herring[‡], S.D. Kachman[§], and D.G. Riley[‡].
[*]USDA, ARS, Roman L. Hruska U.S. Meat Animal Research Center, Clay Center, NE, USA, [†]Pennsylvania State Univ., State College, PA, USA, [‡]Texas A&M Univ., College Station, TX, USA, [§]Univ. of Nebraska, Lincoln, USA

ABSTRACT: Birth weight (**BW**) records of 28,345 Brangus (**BN**) and Simbrah (**SB**) calves (12,252 of which were produced by embryo transfer) were provided by a private seedstock breeder. Objectives were to determine genetic mechanism(s) responsible for 12.3 and 6.9 kg differences in BW between reciprocal F_1 crosses of Brahman (**BR**) and Simmental (**SM**) in male and female embryo transfer calves. The BR X chromosome is estimated to reduce BW by 5.3±1.2 and 4.2±0.9 kg compared to the SM and Angus X in male calves but contributed little to phenotypic variance. The BR X seems preferentially inactivated over the SM X. Gametic imprinting contributed 7.3±1.9 and 3.2±2.1 kg to the reciprocal F_1 effects in SB and BN. The maternal gamete contributed 4.4±2.6 and 5.5±3.5% of phenotypic variance of female and male calves, while the paternal gamete contributed 0 and 1.3±1.6% to female and male calves.

Keywords: Cattle, Gametic Imprinting, X Chromosome

Introduction

Brahman (**BR**) cattle contribute substantially to beef production in the Southern and Southeastern regions of the United States, primarily through crossbreeding and Brahman-influenced composite breeds. Birth weights (**BW**) of calves produced from Brahman sires and *Bos taurus* dams are considerably heavier with greater differences between sexes than calves of the reciprocal cross (Cartwright et al. (1964); Roberson et al. (1986)).

These reciprocal differences were traditionally assumed due to classical maternal effects. However, they have also been observed in reciprocal crosses produced by embryo transfer (**ET**) into similar recipient cows (Baker et al. (1989); Thallman et al. (1992)) and differences among reciprocal backcrosses were documented by Amen et al. (2007). These differences are not consistent with the inheritance models typically assumed in quantitative genetics. Thallman et al. (1992) described several non-traditional genetic models that could explain these effects.

Dillon (2013) estimated that male and female BR × Simmental (**SM**; sire breed listed first in crosses) ET calves were 12.3 and 6.9 kg, respectively, heavier at birth than calves resulting from transfer of SM × BR embryos into comparable recipients. Within BR × SM calves, males were 4.5 kg heavier than females, while SM × BR females were 0.9 kg heavier than the males. The objective is to evaluate which of numerous models best explain these unexpected effects.

Materials and Methods

Data. Birth weight records of 28,345 (**n**) calves born between 1979 and 1991 were provided by Granada BioSciences, Inc., Wheelock, TX. Of these records, 4,969 were in a registered Simbrah (**SB**) breeding program (developed primarily from first crosses) and the remainder were in a registered Brangus (**BN**) breeding program consisting primarily of multi-generation BN. Many combinations of sire and dam breed percentages (of BR and SM) were made in the SB breeding program. The pedigree included 47,354 (**p**) individuals, 7,812 of which were ancestors of SB. The SB data were previously analyzed by Thallman et al. (1992) and Dillon (2013). No purebred Angus (**AN**) or SM and only 35 purebred BR calves (whose foundation BR dams were purchased bred) had BW records suitable for analysis, and they were in contemporary groups that did not include SB or BN.

Of the total, 12,252 calves were produced by ET; 1,316 of those had recipient cows that were registered and had previously produced natural calves (included in this data set) for the registered breeding programs. The remaining recipients were multiparous cows purchased from various sources dry and open with no history. Approximately half of those were straight-bred Holstein (**HO**) dairy cows and the remainder were crossbred beef (**XB**) cows, the majority of which were 25-50% BR. Commercial recipients were classified into one of those two categories, but unfortunately, that information was not transferred along with the remainder of the data for over half the recipient cows; those cows are considered of unknown breed (**UNK**) and assumed to contribute somewhat more variance to their calves' records. The assignment of commercial recipient cows to embryos was random. The assignment of embryos to registered (as opposed to commercial) recipients may not have been random; those two groups of recipients were managed differently at different locations. The distribution of records is in Table 1.

Table 1. Structure of data, birth weight records.

Category	Recipient Type	Recipient Breed	Brangus calves	Simbrah calves
ET	Commercial	Beef	361	201
ET	Commercial	Holstein	1,517	447
ET	Commercial	Unknown	6,270	2,140
ET	Registered	Brangus	1,244	3
ET	Registered	Simbrah	0	69
Non-ET	Dam is Donor		707	288
Non-ET	Natural Dam		13,277	1,821[*]
Total			23,376	4,969

[*]35 were purebred Brahman calves whose dams were purchased bred.
[†]Natural progeny of cows that had been previously flushed for ET.

Statistical analyses. The data were analyzed in ASReml (Gilmour et al., 2009) with the model:

$$\mathbf{y}_f = \mathbf{X\beta} + \mathbf{Z}_{CG}\mathbf{c} + \mathbf{Z}_{DOB}\mathbf{d} + \mathbf{Z}_{HO}\mathbf{r}_{HO} + \mathbf{Z}_{XB}\mathbf{r}_{XB} + \mathbf{Z}_{UNK}\mathbf{r}_{UNK} + \mathbf{Z}_f\mathbf{u}_{Df} + \mathbf{Z}_{mat}\mathbf{u}_M + \mathbf{Z}_f\mathbf{v}_{XMf} + \mathbf{Z}_{sire}\mathbf{v}_{XPf} + [\mathbf{Z}_f : \mathbf{0}]\mathbf{v}_{MEf} + [\mathbf{0} : \mathbf{Z}_f]\mathbf{v}_{PEf} + \mathbf{e}_f$$

$$\text{Var}\begin{bmatrix}\mathbf{c}\\ \mathbf{d}\\ \mathbf{r}_{HO}\\ \mathbf{r}_{XB}\\ \mathbf{r}_{UNK}\end{bmatrix} = \begin{bmatrix}\sigma^2_{CG}\mathbf{I} & \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0}\\ \mathbf{0} & \sigma^2_{DOB}\mathbf{A}\mathbf{R}_1(\rho_{DOB}) & \mathbf{0} & \mathbf{0} & \mathbf{0}\\ \mathbf{0} & \mathbf{0} & \sigma^2_{HO}\mathbf{I} & \mathbf{0} & \mathbf{0}\\ \mathbf{0} & \mathbf{0} & \mathbf{0} & \sigma^2_{XB}\mathbf{I} & \mathbf{0}\\ \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0} & \sigma^2_{UNK}\mathbf{I}\end{bmatrix}$$

$$\text{Var}\begin{bmatrix}\mathbf{u}_{Df}\\ \mathbf{u}_{Dm}\\ \mathbf{u}_M\\ \mathbf{v}_{XMf}\\ \mathbf{v}_{XPf}\\ \mathbf{v}_{XMm}\end{bmatrix} = \begin{bmatrix}\sigma^2_{Df}\mathbf{A} & \sigma_{DfDm}\mathbf{A} & \sigma_{DfM}\mathbf{A} & \mathbf{0} & \mathbf{0} & \mathbf{0}\\ \sigma_{DfDm}\mathbf{A} & \sigma^2_{Dm}\mathbf{A} & \sigma_{DmM}\mathbf{A} & \mathbf{0} & \mathbf{0} & \mathbf{0}\\ \sigma_{DfM}\mathbf{A} & \sigma_{DmM}\mathbf{A} & \sigma^2_{M}\mathbf{A} & \mathbf{0} & \mathbf{0} & \mathbf{0}\\ \mathbf{0} & \mathbf{0} & \mathbf{0} & \sigma^2_{XMf}\mathbf{G}_X & \sigma_{XMfPf}\mathbf{G}_X & \sigma_{XMfMm}\mathbf{G}_X\\ \mathbf{0} & \mathbf{0} & \mathbf{0} & \sigma_{XMfPf}\mathbf{G}_X & \sigma^2_{XPf}\mathbf{G}_X & \sigma_{XPfMm}\mathbf{G}_X\\ \mathbf{0} & \mathbf{0} & \mathbf{0} & \sigma_{XMfMm}\mathbf{G}_X & \sigma_{XPfMm}\mathbf{G}_X & \sigma^2_{XMm}\mathbf{G}_X\end{bmatrix}$$

$$\text{Var}\begin{bmatrix}\mathbf{v}_{MEf}\\ \mathbf{v}_{MEm}\\ \mathbf{v}_{PEf}\\ \mathbf{v}_{PEm}\\ \mathbf{e}_f\\ \mathbf{e}_m\end{bmatrix} = \begin{bmatrix}\sigma^2_{MEf}\mathbf{G}_I & \sigma_{MEfm}\mathbf{G}_I & \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0}\\ \sigma_{MEfm}\mathbf{G}_I & \sigma^2_{MEm}\mathbf{G}_I & \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0}\\ \mathbf{0} & \mathbf{0} & \sigma^2_{PEf}\mathbf{G}_I & \sigma_{PEfm}\mathbf{G}_I & \mathbf{0} & \mathbf{0}\\ \mathbf{0} & \mathbf{0} & \sigma_{PEfm}\mathbf{G}_I & \sigma^2_{PEm}\mathbf{G}_I & \mathbf{0} & \mathbf{0}\\ \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0} & \sigma^2_{ef}\mathbf{I} & \mathbf{0}\\ \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0} & \sigma^2_{em}\mathbf{I}\end{bmatrix}$$

where $\mathbf{y}_f$ is the vector of records of female calves and the model for male calves is similar except the subscript *f* is replaced by *m* and the term, $\mathbf{Z}_{sire}\mathbf{v}_{XPf}$ (for the paternally inherited X chromosome), is omitted.

Non-genetic fixed effects included sex of calf (**Sex**), birth location (**BLOC**), age of dam (**AOD**), ET category (**CAT**), and recipient breed (**RBRD**). Birth location refers to the management unit on which the calf was born; all were within about a 30 km radius, but each was staffed separately. Age of dam was fit as a Legendre polynomial of age in fractional years with linear and quadratic terms. There were four levels of CAT: ET with commercial recipient of unknown background (**ET-C**), ET with registered recipient (**ET-R**), non-ET whose dams had been previously flushed as ET donors (**DON**), and non-ET (**NET**).

Contemporary groups (**CG**; **c**) were fit as a random effect and were defined as combinations of BLOC, CAT (except that DON and NET were combined) and weaning contemporary group (**WCG**). Calves without weaning weights (because they died or were sold prior to weaning) were assigned WCG based on BLOC, CAT, birth date, AOD and tag number. The contemporary group definition precluded ET and NET calves from being in the same contemporary group; this is emphasized because the maternal effects portions of the model differed between these two types of calves. Recipient breed and CG were partially confounded. Non-ET calves were a mixture of AI and natural service, the majority being AI.

Date of Birth (**DOB**; **d**) was fit as a random effect with a level for each day within the range of the data and with a first-order autoregressive variance structure, so that calves born close together in time shared similar effects of birth date. This term was common across all birth locations and was intended to account for seasonal effects and shortterm weather events. Non-genetic random effects were modeled as uncorrelated with the genetic effects.

Random genetic effects were fit separately by sex of calf and included direct additive in male ($\mathbf{u}_{Dm}$) and female ($\mathbf{u}_{Df}$) calves and maternal additive ($\mathbf{u}_M$). The $\mathbf{u}_{Dm}$, $\mathbf{u}_{Df}$, and $\mathbf{u}_M$ effects, and the covariances between them, were modeled as having covariance matrices proportional to the numerator relationship matrix (**A**). For calves except ET-C, maternal permanent environmental effects (**PE**) were modeled as independently and identically distributed (**IID**) and uncorrelated with the random genetic effects. The PE effect was estimated to be zero and subsequently dropped from the model. The $\mathbf{u}_M$ effect was not fit for ET-C calves. Instead, random recipient effects, $\mathbf{r}_{HO}$, $\mathbf{r}_{XB}$, and $\mathbf{r}_{UNK}$ were fit as IID for the records of ET-C calves, with separate variances for each of the three recipient breed categories, HO, XB, and UNK, respectively. Each row of the matrix, $[\mathbf{Z}_{HO}\ \mathbf{Z}_{XB}\ \mathbf{Z}_{UNK}\ \mathbf{Z}_{mat}]$ had exactly one nonzero element (1) such that the maternal contribution to each calf was modelled appropriately with potentially different variance and mean (accounted for by the fixed effect, RBRD).

Random gametic imprinting effects were included by fitting the inverse gametic covariance matrix, $\mathbf{G}_I$, of order 2p × 2p, as described by Schaeffer et al. (1989). The vectors of maternally expressed gametic effects, $\mathbf{v}_{MEm}$ and $\mathbf{v}_{MEf}$, in male and female calves, respectively, each have two elements for each individual in the pedigree. The maternally inherited gametes of all individuals are in the top half of each vector, followed by the paternally inherited gametes in the bottom half. The difference in their expression is modeled through the design matrices. The effects of maternally expressed genes on a male calf are modeled by the term, $[\mathbf{Z}_m : \mathbf{0}]\mathbf{v}_{MEm}$. The n × p matrix, $\mathbf{Z}_m$, relates his maternally inherited copy of any gene that is maternally expressed to his phenotype while $\mathbf{0}_{n\times p}$ indicates that the paternally inherited copies of these genes have no effect on phenotype. Nonetheless, this paternal, bottom half of $\mathbf{v}_{MEm}$ is important; together with $\mathbf{G}_I$, it allows the inheritance of maternally expressed genes to be tracked through sires.

Conversely, $[\mathbf{0} : \mathbf{Z}_m]$ relates paternally expressed genes in the bottom half of $\mathbf{v}_{PEm}$ to his phenotype. Similarly, $[\mathbf{0} : \mathbf{Z}_f]$ relates paternally expressed genes in the bottom half of $\mathbf{v}_{PEf}$ to the phenotype of a female calf. The $\mathbf{G_I}$ matrix and order of effects are identical between $\mathbf{v}_{MEf}$, $\mathbf{v}_{MEm}$, $\mathbf{v}_{PEf}$, and $\mathbf{v}_{PEm}$; it is the scalar variances, σ^2_{MEf}, σ^2_{MEm}, σ^2_{PEf}, and σ^2_{PEm} that the $\mathbf{G_I}$ matrices are multiplied by that reflect the degree of maternal and paternal expression in male and female calves, respectively.

Throughout this paper, the term X chromosome is meant to exclude the pseudo-autosomal region; it is assumed to be accounted for by the other terms in the model that are intended for autosomes. Random X chromosome gametic effects were modeled with an inverse matrix of relationships among X chromosomes at the

gametic level, $\mathbf{G}_X$, of order p × p. This matrix has one row (column) for each individual in the population. The element of $\mathbf{v}_{XMm}$ corresponding to each male represents the one and only X chromosome possessed by that individual. The element of $\mathbf{v}_{XMf}$ corresponding to each female represents the X chromosome that she inherited from her dam, which is potentially recombinant. The female's paternal X chromosome is represented by the element of $\mathbf{v}_{XPf}$ corresponding to her sire; this chromosome cannot be recombinant. Therefore, if the paternal X chromosome effects were modeled in their own row (column) in $\mathbf{G}_X$, each of them would create exactly one dependency with their sire's row (column); this would be pointless.

Each individual's phenotype is related to its element of $\mathbf{v}_{XMf}$ or $\mathbf{v}_{XMm}$ by $\mathbf{Z}_f$ or $\mathbf{Z}_m$, respectively. On the row for a male, $\mathbf{Z}_m$ has one in the individual's column and is zero elsewhere; the same applies to $\mathbf{Z}_f$ for a female. However, a female also has a paternal X chromosome represented by the element of $\mathbf{v}_{XPf}$ for her sire. This is related to her phenotype by $\mathbf{Z}_{sire}$, which has one in her row in the column for her sire. Thus, $\mathbf{Z}_m$, $\mathbf{Z}_f$, and $\mathbf{Z}_{sire}$ each consist of only zeros and ones, with no more than one non-zero element per row and a linear combination of these matrices relates phenotypes to the vector of gametic X chromosome effects, $\mathbf{v}_{XMm}$, $\mathbf{v}_{XMf}$, and $\mathbf{v}_{XPf}$. Under random X-inactivation and equal gene dosage, $\mathbf{v}_{XMf}$ and $\mathbf{v}_{XPf}$ are each expected to contribute about half as much to the phenotype as $\mathbf{v}_{XMm}$ such that σ^2_{XMf} and σ^2_{XPf} are each expected to be about ¼ σ^2_{XMm}. The correlations among the three vectors of X chromosome effects would be expected to be one or close to it. The literature contains many examples of non-random X chromosome inactivation, especially in placental tissues that could plausibly affect BW. Therefore, these assumptions were tested.

This model for fitting the X chromosome differs from that of Fernando and Grossman (1990) implemented by the !XLINK option of ASREML in which each row corresponds to the total X effect of an individual so it would be difficult to assign different effects to the maternal and paternal gametes of a female.

Breed effects were accounted for by genetic covariates designed to model modes of genetic action which may influence the unusual response in BW described in Thallman et al. (1992) and Dillon (2013). All covariates representing genetic effects were probabilities or expected values calculated from pedigree information. In cases where it was not possible to trace pedigree back to purebred individuals, the probabilities were assigned based on the recorded breed composition of the earliest recorded founder.

Breed effects were fit as covariates, in each case as the effect of either SM or AN contrasted with BR. For each breed effect covariate, the subscript, SM or AN, indicates whether the covariate represents a contrast with SM, or AN, respectively. In some cases, a subscript of * may be used to refer to the SM and AN covariates for a model collectively. The following breed effect covariates were included: Direct additive ($\mathbf{D}_{SM}$; $\mathbf{D}_{AN}$), maternal additive ($\mathbf{M}_{SM}$; $\mathbf{M}_{AN}$), direct (**HET**) and maternal (**MHT**) expected breed heterozygosity, gametic imprinting ($\mathbf{GI}_{SM}$; $\mathbf{GI}_{AN}$), probability of non-BR X chromosome ($\mathbf{X}_{SM}$; $\mathbf{X}_{AN}$), probability of non-random X inactivation due to the breed of origin ($\mathbf{NXB}_{SM}$; $\mathbf{NXB}_{AN}$) or parent of origin ($\mathbf{NXP}_{SM}$; $\mathbf{NXP}_{AN}$). For each genetic model, the BR reference point was ensured by fitting a hidden covariate consisting of 1 – P(SM) – P(AN) – P(BR) where P() refers to the probability of breed of origin under that genetic model. These hidden covariates are necessary due to small percentages of other breeds, primarily due to the grading up process for SM and SB cattle. They generally had large standard errors and were considered nuisance parameters; thus, they are not reported.

Interactions of D_*, M_*, HET, MHT, GI_*, and X_* × Sex were tested. Only MHT × Sex was significant and it was retained in the final model. When only the SB subset was analyzed, GI_* × Sex was significant; it was also retained in the final model. The interaction of GI × X_{SM} has been shown to have an effect in mice (Vrana et al. (2000)) and was included although not significant.

Results and Discussion

Non-genetic fixed effects. Table 2 shows the estimates of the fixed effects used to adjust the data and the correlations among those effects. The correlations show that there was very little confounding between the main effects, all of which were highly significant. There were some high

Table 2. Estimates, standard errors, and correlations among non-genetic fixed effects on birth weight, kg.

		Est.,	SE,		Sex	CAT					RBR			AOD	
Effect	Level	kg	kg	P <	Mean	M - F	ET-C	ET-R	DON	NET	HO	UNK	XB	Lin	Quad
Mean		22.7	1.0	0.0000	1	-0.24	-0.37	0.00	0.00	0	0.00	0.00	0	0.35	0.30
Sex	M - F	2.2	0.5	0.0001	-0.24	1	0.03	0.00	0.00	0	0.01	0.00	0	0.00	0.00
CAT	ET-C	7.8	0.8	0.0000	-0.37	0.03	1	0.05	0.00	0	-0.28	-0.32	0	-0.46	-0.40
CAT	ET-R	1.9	0.4	0.0000	0.00	0.00	0.05	1	0.08	0	0.02	-0.04	0	0.05	0.10
CAT	DON	1.0	0.2	0.0000	0.00	0.00	0.00	0.08	1	0	0.00	0.00	0	0.06	0.12
CAT	NET	0.0	0.0		0	0	0	0	0	0	0	0	0	0	0
RBRD	HO	1.2	0.3	0.0001	0.00	0.01	-0.28	0.02	0.00	0	1	0.69	0	0.00	0.00
RBRD	UNK	0.5	0.3	0.1076	0.00	0.00	-0.32	-0.04	0.00	0	0.69	1	0	0.00	0.00
RBRD	XB	0.0	0.0		0	0	0	0	0	0	0	0	0	0	0
AOD	Lin	-6.9	0.5	0.0000	0.35	0.00	-0.46	0.05	0.06	0	0.00	0.00	0	1	0.92
AOD	Quad	-3.6	0.2	0.0000	0.31	0.00	-0.40	0.10	0.12	0	0.00	0.00	0	0.92	1

correlations among levels within main effect. The much higher BW of ET-C relative to calves born to registered cows may partially reflect lower average BR influence in the ET-C recipients, but is completely confounded with CG and definitely also reflects treatment and management differences.

Non-genetic variances. Variance of CG was 3.1±0.3 kg^2. Date of birth explained 2.7±0.6 kg^2 of variance with an autocorrelation between successive days of 0.986±0.003. Table 3 shows variances of maternal effects by type of recipient or natural dam. Heritabilities of ET calves from commercial recipients were a bit lower than those from registered dams.

Population structure. Although the BN and SB populations were owned and managed by the same company, the ways they contribute to this analysis are markedly different. Granada had been breeding BN cattle for several years by 1979 and their herd consisted primarily of multi-generation BN that were at least 3-5 generations from their closest purebred ancestor and over 10 generations along some lines of descent. Granada entered the SB breed in 1983 with the purchase of BR, SM, SM × BR F_1, and SB cows and extensive use of SM and BR AI sires. However, the original SB founder cows had little eventual influence on the herd. Consequently, the SB population is much more powerful for estimation of breed effects through the fixed covariates, while the larger numbers of the BN population make it more powerful for investigating mechanisms through variance structures. In both breeds, the combination of ET and non-ET cattle in the same population was very useful for partitioning genetic mechanisms. In fact, without both, GI_* would have been completely confounded with M_*. Some of the BR foundation cows were bred to AN bulls for breeding new generation BN starting in about 1986.

Table 3. Effect of maternal environments with different maternal variances on phenotypic variance and additive direct heritability and total heritability.

Variance or Heritability	ET-R & NET*	HO Recip.	UNK Recip.	XB Recip.
Maternal var., kg^2	4.1±0.4	13.4±1.2	8.2±0.5	8.3±1.8
Phenotypic var. , $kg^{2\dagger}$	26.9±0.6	39.2±1.3	34.3±0.8	34.4±1.9
Add. heritability, %‡	41.4±4.3	28.4±3.1	32.5±3.4	32.4±3.8
Total heritability, %§	47.5±3.3	32.6±2.4	37.3±2.5	37.1±3.1

*Non-ET calves were equivalent here to registered recipient, except genetic dam and recipient were the same cow.

†Phenotypic variance is sex-averaged and computed for non-ET or calves of registered recipients as:

$$\sigma^2_{Pf} = \sigma^2_{Df} + \sigma^2_{M} + \sigma_{DfM} + \sigma^2_{MEf} + \sigma^2_{PEf} + \sigma^2_{XMf} + \sigma^2_{XPf} + 2\sigma_{XMfPf} + \sigma^2_{ef}$$

$$\sigma^2_{Pm} = \sigma^2_{Dm} + \sigma^2_{M} + \sigma_{DmM} + \sigma^2_{MEm} + \sigma^2_{PEm} + \sigma^2_{XMm} + \sigma^2_{em}$$

For calves with Holstein (HO), crossbred beef (XB), or unknown breed (UNK) recipients, replace $\sigma^2_M + \sigma_{DsM}$ with σ^2_{HO}, σ^2_{XB}, or σ^2_{UNK}, respectively, where $s \in \{m, f\}$. The difference in phenotypic variance between registered and commercial recipients is greater than the apparent respective difference in maternal variance. This is because the additive maternal variance is nearly offset by the negative covariance with additive direct; thus the maternal variance for registered cows adds less to phenotypic variance than it appears on the surface.

‡$(\sigma^2_{Df} + \sigma^2_{Dm})/(\sigma^2_{Pf} + \sigma^2_{Pm})$

§$\dfrac{\sigma^2_{Df} + \sigma^2_{MEf} + \sigma^2_{PEf} + \sigma^2_{XMf} + \sigma^2_{XPf} + 2\sigma_{XMfPf} + \sigma^2_{Dm} + \sigma^2_{MEm} + \sigma^2_{PEm} + \sigma^2_{Xm}}{\sigma^2_{Pf} + \sigma^2_{Pm}}$

Genetic variance components. Table 4 shows the (co)variance component estimates and sampling correlations between them. Direct additive and residual variances were 42 and 34% greater in males than in females. There was little confounding between (co)variance parameters; most was between additive genetic, residual and other parameters. Table 5 shows the partitioning of the phenotypic variance into a number of genetic components. Maternally expressed genes accounted for 4.4±2.6 and

Table 5. Functions of (co)variance estimates.

Function of Variance Components	Estimate (females)	Estimate (males)
Additive direct h^2 ($\sigma^2_{Ds}/\sigma^2_{Ps}$), %	42.4±4.0	40.7±5.3
Additive male-female corr. (σ_{DfDm}) , %	97.4±4.3	
Additive maternal h^2 ($\sigma^2_{M}/\sigma^2_{Ps}$) , %	17.3±1.8	13.6±1.4
Direct-maternal corr. (σ_{DsM}) , %	-51.6±5.9	-56.2±7.0
Maternal gametic h^2 ($\sigma^2_{MEs}/\sigma^2_{Ps}$) , %	4.7±2.6	5.6±3.5
Mat. gametic male-fem. corr. (σ_{MEfm}) , %	74.6±24	
Paternal gametic h^2 ($\sigma^2_{PEs}/\sigma^2_{Ps}$) , %	0	1.3±1.6
X h^2 ($(\sigma^2_{XMf}+\sigma^2_{XPf})/\sigma^2_{Pf}$, $\sigma^2_{XMm}/\sigma^2_{Pm}$) , %	0	0.7±0.9
Phenotypic var., reg. dam $(\sigma^2_{Ps})^\dagger$, kg^2	23.7±0.7	30.2±0.6

*In the subscripts of σ^2, *s* represents sex of calf, e.g. *m* or *f*.

†See footnote to Table 3 for definition of phenotypic variances.

Table 4. Estimates, standard errors, and correlations among (co)variance components of birth weight, kg^2.*

Parm.	Est., kg^2	SE, kg^2	σ^2_{Df}	σ_{DfDm}	σ^2_{Dm}	σ_{DfM}	σ_{DmM}	σ^2_{M}	σ^2_{XMm}	σ^2_{MEf}	σ_{MEmf}	σ^2_{MEm}	σ^2_{PEm}	σ^2_{ef}	σ^2_{UNK}	σ^2_{CG}
σ^2_{Df}	8.6	1.0	1	0.82	0.42	-0.52	-0.31	0.31	-0.04	-0.53	-0.46	-0.20	0.03	-0.65	-0.01	0.05
σ_{DfDm}	10.0	1.1	0.82	1	0.74	-0.49	-0.42	0.34	0.00	-0.44	-0.57	-0.39	0.02	-0.52	0.00	0.04
σ^2_{Dm}	12.3	1.7	0.42	0.74	1	-0.30	-0.39	0.25	0.16	-0.24	-0.43	-0.60	-0.34	-0.27	0.00	0.02
σ_{DfM}	-3.1	0.5	-0.52	-0.49	-0.30	1	0.71	-0.67	0.01	-0.12	-0.09	-0.05	-0.01	0.59	0.01	-0.04
σ_{DmM}	-4.0	0.6	-0.31	-0.42	-0.39	0.71	1	-0.68	0.02	-0.06	-0.13	-0.13	0.05	0.40	0.00	-0.02
σ^2_{M}	4.1	0.4	0.31	0.34	0.25	-0.67	-0.68	1	0.00	-0.10	-0.11	-0.06	-0.01	-0.40	0.12	0.03
σ^2_{XMm}	0.2	0.3	-0.04	0.00	0.16	0.01	0.02	0.00	1	0.02	0.00	-0.47	-0.20	0.03	-0.01	0.00
σ^2_{MEf}	1.1	0.6	-0.53	-0.44	-0.24	-0.12	-0.06	-0.10	0.02	1	0.77	0.33	-0.01	-0.11	-0.01	0.00
σ_{MEmf}	1.0	0.5	-0.46	-0.57	-0.43	-0.09	-0.13	-0.11	0.00	0.77	1	0.65	0.00	-0.02	-0.01	-0.01
σ^2_{MEm}	1.7	0.9	-0.20	-0.39	-0.60	-0.05	-0.13	-0.06	-0.47	0.33	0.65	1	0.24	-0.01	0.01	-0.01
σ^2_{PEm}	0.4	0.5	0.03	0.02	-0.34	-0.01	0.05	-0.01	-0.20	-0.01	0.00	0.24	1	-0.02	0.01	0.00
σ^2_{ef}	12.3	0.4	-0.65	-0.52	-0.27	0.59	0.40	-0.40	0.03	-0.11	-0.02	-0.01	-0.02	1	-0.20	-0.09
σ^2_{em}	16.1	0.8	-0.45	-0.43	-0.30	0.43	0.34	-0.30	0.03	-0.05	0.00	-0.02	-0.03	0.65	-0.16	-0.06

*Correlations among the estimates of σ^2_{XB}, σ^2_{HO} , σ^2_{DOB}, and ρ_{DOB}, with the exception of corr(σ^2_{DOB}, ρ_{DOB}) = 0.77, had a maximum absolute value of 0.10.

5.5±3.5% of phenotypic variation in females and males, respectively. Variances of X chromosomal inheritance pattern and paternally expressed genes in female calves were estimated as zero and were dropped from the final model.

Genetic fixed effects. Table 6 shows estimates of genetic fixed effects used to discern genetic mechanisms. The estimates of 5.3±1.2 and 4.2±0.9 kg for X_{SM} and X_{AN} are large and highly significant. A male calf with a BR X chromosome is predicted to weigh 5.3±1.2 kg less than an otherwise similar calf with a SM X chromosome. The significant effect of 3.0±1.0 kg for NXB_{SM} can be thought of as a dominance effect in female calves. A female calf with one BR and one SM X chromosome is expected to weigh ½ × 5.3 + 3.0 = 5.7 kg more than one with two BR X chromosomes; an otherwise similar female with two SM X chromosomes is expected to weigh 5.3 kg more than one with two BR X. The implication is that the SM X is less likely to be inactivated than the BR X. The apparent overdominance is likely a statistical artifact; NXB_{AN} was much smaller and not significant.

The highly significant estimate of GI_* suggests that a SM × BR calf would weigh 7.3±1.9 kg less than a hypothetically otherwise similar (direct, maternal, X, etc.) BR × SM calf. This estimate goes a long way toward explaining the F_1 reciprocal cross effect in ET calves, especially when combined with X_{SM}. However, it is puzzling that so little variance was explained by the X chromosome and gametic imprinting inheritance patterns.

An abundance of caution was exercised in dropping non-significant effects (e.g., D_{SM}, M_{SM}, and MHT) from the model, if those effects would ordinarily be expected to affect BW in cattle. Dropping such model components based only on significance level implicitly assumes that their effects are known to be zero, artificially reduces the standard errors of other model components, and precludes the possibility of examining partial confounding with other terms in the model. For example, the correlation between the estimates of X_{SM} and GI_{SM} × Sex was -0.77. These are two of only three effects in the final model that could plausibly explain the sexual dimorphism that occurs in reciprocal F_1 calves.

Nonetheless, some potential models for the reciprocal cross effect were initially evaluated and then

Table 6. Estimates, standard errors, and correlations among genetic fixed effects on birth weight, kg.

Effect	Est., kg	SE, kg	P <	D_{SM}	D_{AN}	M_{SM}	HET	MHT	GI_{SM}	GI_{AN}	X_{SM}	X_{AN}	NXB_{SM}	GI_{SM} ×Sex	X_{SM} ×Sex
D_{SM}	1.6	1.8	0.3894	1	0.25	-0.30	0.05	-0.05	0.24	0.06	-0.64	0.01	0.09	0.45	-0.03
D_{AN}	-4.5	1.9	0.0173	0.25	1	-0.16	-0.10	-0.06	0.06	0.00	0.06	-0.60	-0.25	-0.05	0.01
M_{SM}	-1.0	1.1	0.3537	-0.30	-0.16	1	-0.03	-0.09	-0.19	-0.09	-0.06	-0.02	0.01	0.07	-0.08
M_{AN}*	3.2	1.0	0.0017	-0.16	-0.30	0.63	-0.04	-0.09	-0.23	-0.15	-0.05	-0.04	0.04	0.05	-0.03
HET	2.9	1.0	0.0052	0.05	-0.10	-0.03	1	0.24	0.13	0.11	-0.12	-0.09	0.72	0.11	-0.04
MHT	0.6	0.4	0.1705	-0.05	-0.06	-0.09	0.24	1	0.06	0.02	0.00	-0.01	0.12	0.00	0.00
GI_{SM}	7.3	1.9	0.0001	0.24	0.06	-0.19	0.13	0.06	1	0.03	-0.37	-0.02	0.03	0.36	-0.04
GI_{AN}	3.2	2.1	0.1267	0.06	0.00	-0.09	0.11	0.02	0.03	1	-0.01	-0.06	0.05	0.01	0.00
X_{SM}	5.3	1.2	0.0001	-0.64	0.06	-0.06	-0.12	0.00	-0.37	-0.01	1	0.01	-0.20	-0.78	0.21
X_{AN}	4.2	0.9	0.0000	0.01	-0.60	-0.02	-0.09	-0.01	-0.02	-0.06	0.01	1	-0.08	-0.03	0.05
NXB_{SM}	3.0	1.0	0.0014	0.09	-0.25	0.01	0.72	0.12	0.03	0.05	-0.20	-0.08	1	0.14	-0.03
NXB_{AN}*	1.3	1.1	0.2453	-0.02	0.45	0.05	0.27	0.05	0.04	-0.25	-0.02	-0.34	0.26	0.02	0.01
NXP_{SM}*	0.2	0.7	0.7450	-0.03	-0.02	0.06	-0.11	-0.09	-0.77	0.01	0.09	0.03	-0.13	-0.04	-0.19
NXP_{AN}*	-0.2	0.6	0.6706	0.00	0.13	0.01	0.08	0.02	0.01	-0.57	-0.01	-0.15	0.06	0.06	-0.14
GI_{SM}×Sex	0.7	1.5	0.6545	0.45	-0.05	0.07	0.11	0.00	0.36	0.01	-0.78	-0.03	0.14	1	-0.43
GI_{AN}×Sex*	3.0	2.1	0.1489	-0.01	0.30	0.00	0.02	0.00	0.01	0.13	0.01	-0.47	0.01	0.04	-0.16
X_{SM}×Sex	1.5	1.0	0.1281	-0.03	0.01	-0.08	-0.04	0.00	-0.04	0.00	0.21	0.05	-0.03	-0.43	1
X_{AN}×Sex*	0.5	0.8	0.5296	-0.02	0.06	-0.01	-0.05	0.00	0.00	0.00	0.06	0.04	-0.01	-0.32	0.75
MHT×Sex*	-1.1	0.2	0.0001	0.06	-0.01	-0.01	0.00	0.05	0.00	0.00	-0.09	-0.01	0.01	0.04	-0.07

*Columns for M_{AN}, MHT×Sex, NXB_{AN}, NXP_{SM}, NXP_{AN}, GI_{AN}×Sex, and X_{AN}×Sex not shown. The highest absolute value of correlation between the estimates of these effects and any effect above the diagonal (and hence, not shown) was 0.21.

Table 7. Correlations between non-genetic and genetic fixed effects on birth weight, kg.

Effect	Level	D_{SM}	D_{AN}	M_{SM}	HET	MHT ×Sex	GI_{SM}	GI_{AN}	X_{SM}	X_{AN}	NXB_{SM}	GI_{SM} ×Sex	X_{SM} ×Sex
Mean*		-0.21	-0.26	-0.12	-0.23	-0.19	0.02	-0.03	0.02	0.01	0.06	-0.08	0.19
Sex	M - F	0.00	-0.01	0.02	0.05	0.00	0.00	0.00	-0.04	-0.06	0.01	0.34	-0.78
CAT	ET-C	-0.16	-0.20	0.49	0.03	0.22	-0.18	-0.11	-0.04	-0.03	0.05	0.04	-0.02
CAT	ET-R	-0.01	0.04	-0.02	-0.01	-0.01	0.01	0.01	0.00	0.00	-0.01	0.00	0.00
CAT	DON	-0.01	0.00	-0.08	0.01	-0.01	-0.02	0.00	0.03	0.00	0.02	-0.02	0.01
CAT	NET	0	0	0	0	0	0	0	0	0	0	0	0
RBRD	HO	0.00	0.00	-0.02	0.01	0.00	0.02	0.02	0.00	0.00	0.01	-0.01	0.00
RBRD	UNK	0.01	0.00	-0.03	0.01	-0.01	0.01	0.02	0.00	0.00	0.02	-0.01	0.00
RBRD	XB	0	0	0	0	0	0	0	0	0	0	0	0
AOD	Lin	0.01	0.02	0.00	0.00	-0.01	0.01	0.01	-0.01	-0.01	-0.01	0.01	0.00
AOD	Quad	0.01	0.01	-0.03	0.02	0.01	0.02	0.01	-0.01	-0.01	0.00	0.01	0.00

*BLOC is not shown. There are high correlations among estimates of levels of BLOC and moderate correlations of BLOC with the mean. Otherwise, the highest absolute value of correlation between the estimates of BLOC and any other non-genetic or genetic factor is 0.06.

discarded. Both the Y chromosome and mitochondrial DNA are appealing models to explain a reciprocal cross effect and, in the case of Y chromosome to explain sexual dimorphism. Pedigrees were traced back to purebred founders where possible and both fixed breed effects and variance of random founder effects were all estimated to be essentially zero. As these are not models that are generally expected to affect birth weight, they were dropped from the final model.

In the SB analysis of Dillon (2013), both NXB_{SM} and NXP_{SM} were partially confounded with various other effects, including X_{SM}, and their significance varied greatly depending on what else was in the model. It appeared likely that the X chromosome had an effect and quite possible that non-random inactivation was involved, but it was ambiguous. Adding the BN data and fitting variance models provided a clearer picture.

The breed differences between AN and SM were estimated only very indirectly and were expected to have large standard errors. Contrasts between them (not shown) were surprisingly large with surprisingly small standard errors. Nonetheless, they are subject to being influenced by extraneous effects not included in the model and it is suggested that they be viewed with extreme caution.

Correlations between genetic and non-genetic fixed effects. Table 7 shows areas of potential confounding. Together with Tables 2 and 7, it provides sufficient information to estimate and test any contrast among the fixed effects. The only areas of concern are the negative correlations between the additive maternal effects (M_{SM} and M_{AN}) and CAT and the negative correlations between Sex and X_{SM}×Sex. These correlations provide at least a potential explanation for the puzzling estimates of these genetic effects. There is no indication of confounding of GI_{*}, X_{*}, or NXB_{SM} with any non-genetic component of the model.

Sex-specific effects. The much higher residual variance for males than for females is a bit puzzling, but perhaps enlightening. Preliminary versions of the model did not contain sex-specific random effects, except for the X chromosome, where it was speculated that departures from the standard assumptions of X-inactivation could be expected. But even in that case, it was assumed that the effects of X chromosomes would differ only by scaling; that $\mathbf{v}_{XMm}$, $\mathbf{v}_{XMf}$, and $\mathbf{v}_{XPf}$ would be proportional to each other. Under such model, σ^2_{XMm} was estimated to be 21% of phenotypic variance; this was unexpected and raised the question of whether males might have greater residual variance than females. The male residual variance has been estimated to be as much as 50% higher than the female, depending on what else is in the model. It appears likely that much of the additional variance of males is due to genetic (probably some form of epistasis) variation that is expressed in males, but not in females. This could be due to inter-actions with testosterone or some other factor that is explicitly male in nature. Additional analyses will need to be devised to unravel more of this genetic mystery. However, the current results point in a direction that has probably not been explored substantially in previous efforts to under-stand the reciprocal cross effect and sexual dimorphism.

Conclusions

The X chromosome and gametic imprinting appear to have important effects on BW in BR × *B. taurus* crosses, together accounting for 13.0 and 6.7 kg of the SB F_1 reciprocal cross difference in males and females, respectively. It appears X chromosome inactivation is non-random with respect to breed of origin. Together, X_{SM}, NXB_{SM}, , and GI_{SM} × Sex accounted for 6.3 kg of the 5.4 kg sexual dimorphism in reciprocal F_1 crosses of BR with SM. These results may guide the search for genomic regions containing the genes responsible for these effects (which have been surprisingly elusive in searches thus far).

These results suggest that X chromosome inheritance and gametic imprinting should be considered in genetic evaluation of Brahman-influenced cattle and that genomic selection on breed-of-origin, especially for the X chromosome, could be highly effective in Brahman-influenced composites or breeds. At least from the perspective of birth weight, crossbreeding programs should emphasize Brahman contribution to the maternal part of a breeding system and *B. taurus* to the paternal part. Finally, it seems plausible that introgression of the Brahman X chromosome (or portions of it) and potentially limited autosomal regions responsible for major fractions of the gametic imprinting × sex effect into *B. taurus* breeds could provide a mechanism for reducing dystocia relative to growth rate through reducing sexual dimorphism for BW.

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