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Genomic imprinting significantly contributes to genetic variability of 19 traits in slaughter pigs

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Genomic imprinting refers to an epigenetic marking of genes which are differentially expressed from the maternally and paternally inherited alleles. So the laws of Mendel are apparently switched off. The first molecular evidence for imprinting in mammals was found in the middle of the 1980s. The molecular mechanism is a parent-specific methylation of DNA, established during gametogenesis. A lot of studies have shown that imprinting plays a role in many aspects of development, cell proliferation, adult behavior and some diseases. A special type of imprinting, known as partial imprinting, influences allele expression in one or several of the following ways: it is possible that an allele is understated in its expression. A second possibility is the cell-type-specific allele expression. In another variation the expression is changed in different phases of life.

A lot of QTL and imprinting analyses exist, which reported about imprint alleles. IGF2 was identified as an important imprinted gene in pigs. In the first studies of imprinting in farm animals the variance components were estimation (De Vries et al., 1994). Engellandt and Tier (2001) found significant effects of paternal gametes in two fatness traits of finishing bulls. Essl and Voith (2002) estimated the variance of imprinting effects on dairy- and fitness-related traits of cattle. Therefore, we are interested in the relative portion of the additive genetic variance induced by imprinted genes.

Material and Method

The dataset was provided by Suisag Switzerland. Edelschwein is the most important breed in Switzerland. The slaughter data were derived from their herd book breeding program. Between 1997 and 2006 in total 21,209 pig data were recorded. The data set comprised 35 traits from three groups: growth traits (6), quality traits (3) and carcass traits (26).

A linear mixed model with the following effects was fitted to each trait and variance components were estimated via REML:

$$Y_{ijklmnopqr} = S_i + B_j + b_1 x_1 + p_k + f_l + l_m + y_n + m_o + s_p + d_q + e_{ijklmnopqr}$$

$Y_{ijklmnopqr}$ = trait

S_i = sex (fix) (i = 1, 2)

B_j = barn*cycle (fix) (j = 1,..., 374)

b_1 = linear regression on the slaughter weight

p_k = pen (random) (k = 1,…, 3847)

f_l = farm of origin (random) (l =1,…, 678)

l_m = litter (random) (m = 1,…, 8887)

y_n = y-chromosomal inheritance (random) (p = 1, …, 71)

m_o = mitochondrial inheritance (random) (q = 1, …, 331)

s_p = additive genetic effect as sire (random) (n = 1, ..., 15747)

d_q = additive genetic effect as dam (random) (o = 1, ..., 15747)

$e_{ijklmnopqr}$ = random residuals

With the additive genetic effect as sire and as dam, we estimated two breeding values for each animal, using the following animal model: $y = X\beta + Z_s a_s + Z_d a_d + e$

The structure of the mixed model equations are as follows:

$$\begin{bmatrix} X'W^{-1}X & X'W^{-1}Z_s & X'W^{-1}Z_d \\ Z'_s W^{-1}X & Z'_s W^{-1}Z_s + A^{-1}\alpha_1 & Z'_s W^{-1}Z_d + A^{-1}\alpha_2 \\ Z'_d W^{-1}X & Z'_d W^{-1}Z_s + A^{-1}\alpha_2 & Z'_d W^{-1}Z_d + A^{-1}\alpha_3 \end{bmatrix} \begin{bmatrix} \beta \\ a_s \\ a_d \end{bmatrix} = \begin{bmatrix} X'W^{-1}y \\ Z'_s W^{-1}y \\ Z'_d W^{-1}y \end{bmatrix}$$

y = vector of observations

X = design matrix for fixed effects

β = vector of fixed effects

A = additive genetic relationship matrix of parents only

Z_s, Z_d = design matrix for random effects

a_s = vector for breeding values with paternal expression pattern

a_d = vector for breeding values with maternal expression pattern

W is a diagonal matrix with appropriate weights in order to account for the inbreeding coefficients of the parents: $w_i = \left[\frac{1/2\,\sigma_s^2(1-F_{si}) + 1/2\,\sigma_d^2(1-F_{di}) + \sigma_e^2}{1/2\,\sigma_s^2 + 1/2\,\sigma_d^2 + \sigma_e^2} \right]^{-1}$

The variance of the random effects is:

$$Var\begin{bmatrix} a_s \\ a_d \\ e \end{bmatrix} = \begin{bmatrix} 1/2\,A\sigma_s^2 & 1/2\,A\sigma_{sd} & 0 \\ 1/2\,A\sigma_{sd} & 1/2\,A\sigma_d^2 & 0 \\ 0 & 0 & W\sigma_e^{2^*} \end{bmatrix}$$

Where σ_s^2 and σ_d^2 are the gametic variances for the genetic effects as sire and as dam, respectively, and σ_{sd} is its covariance.

If imprinting is present, then S* is positive definite:

$$S^* = \begin{bmatrix} \sigma_s^2 & \sigma_{sd} \\ \sigma_{sd} & \sigma_d^2 \end{bmatrix}$$

and in the absence of imprinting S* is not positive definite:

$$S^* = \begin{bmatrix} \sigma_g^2 & \sigma_g^2 \\ \sigma_g^2 & \sigma_g^2 \end{bmatrix}$$

A REML likelihood ratio test with two degrees of freedom was used to test the hypothesis of imprinting against the absence of imprinting. For significantly imprinted traits the imprinting variance (σ_i^2) can be calculated as $\sigma_i^2 = \sigma_s^2 + \sigma_d^2 - 2\sigma_{sd}$ and the total additive genetic variance is $\sigma_a^2 = \sigma_s^2 + \sigma_d^2$.

Parental contributions to imprinting variance can be calculated as $\sigma_m^2 - \sigma_{sd}$ (maternal) and $\sigma_s^2 - \sigma_{sd}$ (paternal).

Results and Discussion

The analyses showed significant imprinting for 19 traits. Up to 19 % of the total additive genetic variance was due to imprinting in these 19 traits. The proportion of parental contributions to the imprinting variance varied widely between traits. They ranged from nearly no maternal contribution to the imprinting variance (H_{30}) to nearly no paternal contribution to the imprinting variance (total feed consumption) (see Figure).

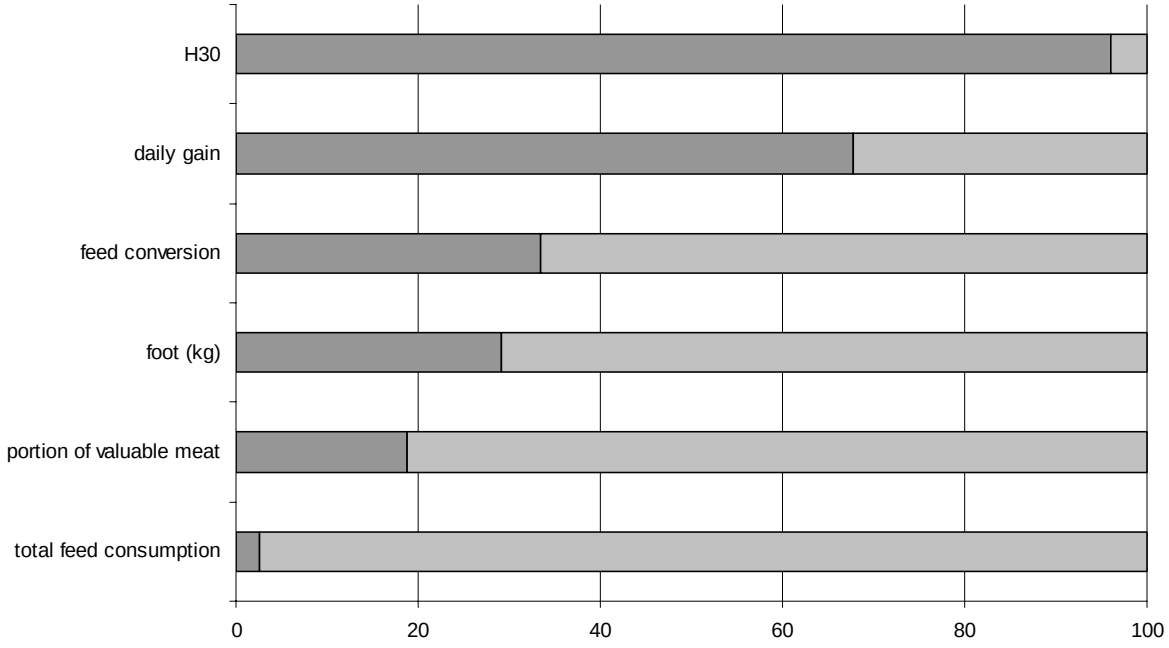

Figure: parental contribution to the imprinting variance. The X-axis presents the different contributions in percent. The dark-grey show the paternal contribution, the light grey the maternal contribution to imprinting for each trait.

The imprinting effect for each animal is the difference between the breeding values per animal. For example in daily gain a lot of the differences exceed 10 g per day.

The questions arise, whether the separation of the imprinting variance from other variances is possible. It is no problem for e.g. the y-chromosomal effect or mitochondrial effect, because they have different correlation structures. But it is impossible, when maternal effects are present, because the maternal effects and the breeding values as dam have a common correlation structure. Therefore, the estimates of the imprinting variance can be interpreted as upper bounds and may be contaminated by a maternal variance contribution. But even in this case the model with two breeding values per animal remains applicable.

Literature

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