

SEGREGATION RATIO OF ESTROGEN RECEPTOR GENOTYPES IN PIG LITTERS FROM LARGE WHITE DERIVED LINES

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INTRODUCTION

In pigs, the estrogen receptor (*ESR*) locus (two alleles, A and B) has been found to be associated with litter size. Dependent on the line, either the B allele (Southwood *et al.*, 1995; Rothschild *et al.*, 1996; Short *et al.*, 1997) or A allele (Van Rens *et al.*, 2002) was favorable. A physiological study of Meishan synthetic AA and BB gilts (in which the B allele was the favorable allele for litter size) showed that the difference in litter size was likely due to a difference in fetal survival through an effect on placental size (Van Rens *et al.*, 2000). In these gilts, several reproductive traits and relations between traits at day 35 of pregnancy were dependent on both maternal and fetal *ESR* genotype (Van Rens and van der Lende, 2000). Since in AA gilts the fraction of day 35 AA fetuses that were growth retarded was larger than the fraction of their AB littermates, a distortion in genotype ratio at birth was suggested (Van Rens and van der Lende, 2000). In the present study this hypothesis was tested in two LW derived lines for all parent genotype combinations that result in more than one genotype being present in their litters. In addition we tested for an effect of mating type (genotype combination of sire and dam) on litter genotype ratio in litters with the same expected genotype proportions.

MATERIAL AND METHODS

ESR genotypes were obtained on animals from 2 pig lines (1 and 2) of Large White origin which had a large number of genotypes available and had intermediate *ESR* allele frequencies. Favorable effects of *ESR* allele B on litter size have previously been shown in a dataset which included these lines (Short *et al.*, 1997). Allele substitution effects reported were 0.42 and 0.31 for TNB in first and later parities respectively. No line**ESR* interaction was found and allele substitution effects were reported to be similar for all lines (Short *et al.*, 1997). For this study, litters were selected that had *ESR* genotype information on both parents and on at least 85% of the born alive offspring. Dead born pigs were included in the analyses when genotypes were available. The whole litter was removed if one or more of the offspring genotypes was inconsistent with parent genotypes. The number of piglets included are shown in table 1 of the results.

Segregation ratios. Segregation ratios were tested for distortion within mating types where at least one of the parents was heterozygous for *ESR* (see table 1 for mating types). Segregation ratios were tested across all parities and separately for first parity offspring. Distortion from expected segregation ratios was tested by χ^2 analysis of the combined set of offspring within each mating type.

Parent-offspring genotype interaction. The effect of parent genotypes on segregation ratio of offspring genotypes was tested by comparing the average ratio of litters from mating type 1 with litters from mating type 2 and between litters from mating type 4 and mating type 5. For this test all parities were used. In the compared mating types, the parent genotype combination is opposite for sire and dam but the expected mixture of offspring genotypes is the same. These are the only comparisons where a difference in segregation distortion can be attributed to the parent genotypes. The following model (SASTM procedure GLM):

$$\text{proportion of AB animals} = \text{mating type} + e$$

was used to test for an effect of mating type on AB proportion (which is expected to be 0.5 in all mating types considered) in a litter. AB proportion was calculated as the number of AB offspring divided by the total number of genotyped offspring within a litter. Least square means for the AB proportion were estimated from this model. An effect of total number born (TNB) and parity on the proportion of AB animals was tested in a preliminary model.

RESULTS

Segregation ratios. Highly significant segregation distortions at birth were found in both lines, especially when looking at the proportions across parities (Table 1).

Table 1. Genotype ratios in offspring from Large White derived lines

type	Matings ^A Sire/Dam/ Off.	Line 1				Line 2			
		N ^B		ratio ^C		N		ratio	
		p1	all ^D	p1	all	p1	all	p1	all
1)	BB / AB / BB	1088	2157	0.50	0.49	839	2759	0.50	0.50
	AB	1078	2232	0.50	0.51	855	2725	0.50	0.50
2)	AB / BB / BB	708	1189	0.51	0.49	668	1660	0.52	0.56^c
	AB	687	1218	0.49	0.51	609	1312	0.48	0.44^c
3)	AB / AB / BB	826	1668	0.20^c	0.21^c	268	654	0.27^a	0.26^b
	AB	2059	4118	0.51^c	0.51^c	501	1281	0.51^a	0.52^b
	AA	1164	2252	0.29^c	0.28^c	214	539	0.22^a	0.22^b
4)	AB / AA / AB	1337	2720	0.48	0.49^a	55	181	0.54	0.52
	AA	1426	2887	0.52	0.51^a	46	164	0.46	0.48
5)	AA / AB / AB	918	1752	0.46^a	0.45^c	29	109	0.57	0.56
	AA	1063	2148	0.54^a	0.55^c	22	87	0.43	0.44

^A ESR genotype combinations of sire and dam. ^B Number of offspring in each class. ^C Ratios of offspring genotype classes. ^D p1: results from first parities, all: results across parities. Significant distorted ratio's (χ^2 test) are indicated in bold. a: $p < 0.05$, b: $p < 0.005$; c: $p < 0.0005$.

Results in first parity offspring and across all parities correspond very well in size and direction of the observed distortions but results from first parities generally reach lower

significance thresholds. Mating types in line 1 which produce AA offspring show significant distortions in *ESR* segregation with decreased proportions of AB or BB genotypes. In line 2, AB or AA offspring were under-represented in 2 out of 3 mating types that produce offspring of BB genotype. In both lines, highly significant distortions were found in mating type 3 where potentially 3 different genotypes are present in the same litter.

Parent-offspring genotype interaction. Littersize (TNB) and parity were not found to have an effect on the segregation ratio when added to the model used to test for parent-offspring genotype interactions. The only significant difference in the amount of distortion is found in the comparison of mating types 4 and 5 of line 1. The proportion of AB offspring is lower than 50% for both mating types 4 and 5 but the amount of the distortion is significantly greater in mating type 5. This difference is interpreted as an interaction of parent and offspring genotype on survival or mortality before birth. In line 2, mating type 2 shows significant distortion while mating type 1 does not. The amount of segregation distortion in mating types 1 and 2 in line 2 is however not significantly different. For the remaining 2 comparisons no significant distortion was found in the individual mating types and as expected, they are also not significantly different from each other.

Table 2. Effect of parent genotype combination on litter *ESR* ratio

mating type	Line 1		Line 2	
	proportion AB ^A	p ^B	proportion AB	p
1	0.51 (0.01)	0.99	0.49 (0.01)	0.19
2	0.51 (0.01)		0.46 (0.01)	
4	0.49 (0.01)	0.02	0.54 (0.04)	0.65
5	0.46 (0.01)		0.57 (0.05)	

^A Proportion AB are least squares means estimates with standard errors.

^B significance value for a difference in AB proportions between mating types 1 and 2 or between mating types 4 and 5.

DISCUSSION

Two Large White derived lines, known to have a positive effect of the *ESR* B allele on littersize, are shown to have distorted segregation ratios for the *ESR* locus at birth in several mating types. This implies that the effect of *ESR* genotype on littersize could, at least partly, be due to an effect of the offspring genotypes on survival to birth. The under-represented genotypes were not the same between lines and were not under-represented for all mating types which means that offspring genotype is not the only factor affecting the genotype ratio distortion. In fact, in line 1, a significant difference in the amount of distortion was seen between mating types 4 and 5 which have the same expected mixture of offspring genotypes. A significant effect of mating type on AB proportion was interpreted as an interaction of mating type and offspring genotype on survival to birth. A plausible explanation for this interaction is an interaction with the genotype of the dam because maternal effects are known to play a larger role than paternal effects, although neither can be ruled out from the results presented here.

In a line where the B allele was favorable for litter size, Van Rens and van der Lende (2000) reported physiological differences between AA and AB fetuses at day 35 that put the AA offspring at a higher risk to die before birth. This was suggested to result in lower proportions of AA offspring at birth. The results in Line 2 confirm this suggestion with reduced proportions of AA offspring in all mating types that produce them. These results were only significant in mating type 3 but types 4 and 5 have limited observations. No significant interaction between parent and offspring genotypes was found in line 2. In line 1, BB or AB piglets were under-represented in mating types with significant distortions. The B allele seems to reduce survival to birth in this line, opposite to line 2 results. The association of the *ESR* polymorphism with litter size have not always been found to be in the same direction. This indicates that the *ESR* polymorphism is most likely not causing these differences in litter size (Van Rens *et al.*, 2002) but rather that the *ESR* polymorphism is in linkage disequilibrium with (additional) causative polymorphism(s). The differences in segregation ratios between lines 1 and 2 indicate that the same could be true for the association of *ESR* with survival to birth.

At this point it is very difficult to give a biological explanation for these intriguing results. The dam's *ESR* and/or background genotype will probably play a role through maternal traits such as uterine capacity and early placental development. Paternal effects, for instance through imprinting, cannot be ruled out. Use of *ESR* genotypes in genetic improvement should be based on its estimated effects on the economic trait of interest, which, in relation to *ESR*, is in most cases litter size.

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