Selection for ovulation rate in rabbits: Genetic parameters and correlated responses on survival rates

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J ANIM SCI 2012, 90:439-446.
doi: 10.2527/jas.2011-4219 originally published online September 16, 2011

Selection for ovulation rate in rabbits: Genetic parameters and correlated responses on survival rates[1]

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ABSTRACT: The aim of this work was to evaluate the correlated responses on survival rates after 10 generations of selection for ovulation rate (OR). Selection was based on the phenotypic value of ovulation rate estimated at d 12 of second gestation by laparoscopy. Traits recorded were litter size (LS), estimated as total number of rabbits born per litter in up to 5 parities; OR, estimated as the number of corpora lutea in both ovaries; the number of implanted embryos (IE), estimated as the number of implantation sites; the number of right and left IE (RIE and LIE); ovulatory difference (OD), defined as the difference between the right and the left OR, expressed as an absolute value; implantatory difference (ID), defined as the difference between RIE and LIE, expressed as an absolute value; embryonic survival (ES), calculated as IE/OR; fetal survival (FS), calculated as LS/IE; prenatal survival (PS), calculated as LS/OR. A total of 1,081 records were used to analyze ES, and 770 were used to analyze FS and PS. The number of records used to analyze the other traits ranged from 1,079 for ID to 3,031 for LS. Data were analyzed using Bayesian methodology. Genetic parameters of OR, OD, and LS were estimated in a previous paper. Estimated heritabilities of IE, ID, ES, FS, and PS were 0.11, 0.03, 0.09, 0.24, and 0.14, respectively. Estimated repeatabilities of IE, ID, and ES were 0.22, 0.12, and 0.20. Estimated phenotypic correlations of OR with ES, FS, and PS were −0.07, −0.26, and −0.28, respectively. Their estimated genetic correlations with FS and PS were negative (probability of being negative 1.00 and 0.98, respectively). Nothing can be said about the sign of the genetic correlation between OR and ES. Ovulation rate was phenotypically uncorrelated with ID. Their estimated genetic correlation was positive (probability of being positive 0.91). The genetic correlation of ID with PS and LS was not accurately estimated. Phenotypic and genetic correlations between LS and survival rates were positive (probability of being positive 1.00). In 10 generations of selection, FS decreased around 1% per generation. No correlated response in ES was observed. In summary, the decrease in FS in rabbits selected for OR seemed to be responsible for the lack of correlated response observed in LS.

Key words: litter size, ovulation rate, rabbit, selection, survival rate

J. Anim. Sci. 2012. 90:439–446
doi:10.2527/jas.2011-4219

INTRODUCTION

Selection for ovulation rate has been proposed as an indirect way of increasing litter size (Zimmerman and Cunningham, 1975); ovulation rate is the upper limit of litter size and has a higher heritability. Laborda et al. (2011) have shown that selection for ovulation rate has been successful in rabbits, but there has been no correlated response in litter size. The same phenomenon has been observed in the experiments of selection for ovulation rate in pigs (Cunningham et al., 1979; Leymaster and Christenson, 2000; Rosendo et al., 2007) and mice (Bradford, 1969; Land and Falconer, 1969). In these selection experiments, the lacking correlated response in litter size was associated with an increase in prenatal mortality. There is little information about the timing of prenatal mortality in experiments of selection for ovulation rate in pigs and mice, due to the difficulties in measuring the number of fetuses without altering litter size. In mice, Bradford (1969) observed that most prenatal mortality occurred after implantation. In pigs, the main difference in prenatal mortality in a line selected for ovulation rate was observed dur-

[1]This study was supported by the Comisión Interministerial de Ciencia y Tecnología CICYT-AGL2005-07624-C03-01 and by funds from the Generalitat Valenciana research programme (Prometeo 2009/125). The authors thank one of the referees for the detailed revision of the manuscript and to R. Peiró and J. P. Sánchez (both from Instituto de Ciencia y Tecnología Animal, Valencia, Spain) for their help with the computer programs.

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Received April 28, 2011.
Accepted September 12, 2011.

ing the early fetal development between d 25 and 45 of gestation (Freking et al., 2007). This difference was associated with less endometrial space for the fetuses at implantation in the selected females. Although pigs and mice have a different uterine architecture and different types of placentation, fetal survival has decreased with selection for ovulation rate in both species.

In rabbits, unlike pigs and mice, it is possible to easily measure the number of implanted embryos by laparoscopy in live females, and thus it is possible to calculate embryonic survival and fetal survival in the same doe without altering litter size (Santacreu et al., 1990). The aim of this study was to evaluate the correlated responses on embryonic survival, fetal survival, and prenatal survival in a rabbit line selected for ovulation rate during 10 generations.

MATERIALS AND METHODS

All experimental procedures involving animals were approved by the Polytechnic University of Valencia Research Ethics Committee.

Animals

Animals belonged to a 10-generation selection experiment for ovulation rate, described in a companion paper by Laborda et al. (2011), which began in February 2002 and continued until February 2010. Selection was based on the phenotypic value of ovulation rate estimated at d 12 of second gestation by laparoscopy. Implantation in rabbits takes place at d 7, and laparoscopy permits counting implantation sites at d 12 (Santacreu et al., 1990).

Traits

Litter size (**LS**) was measured as the total number of kits born per litter; it was measured in a maximum of 5 parities in each female. Ovulation rate (**OR**), estimated as the number of corpora lutea in both ovaries, and the number of implanted embryos (**IE**), estimated as the number of implantation sites, were measured by laparoscopy at d 12 of second gestation. Both the right and the left IE (**RIE** and **LIE**) were measured. Ovulatory difference (**OD**) was defined as the difference between the right and the left OR, expressed as an absolute value; implantatory difference (**ID**), was defined as the difference between RIE and LIE, expressed as an absolute value. Embryonic survival (**ES**) was calculated as IE/OR, fetal survival (**FS**) was calculated as LS/IE, and prenatal survival (**PS**) was calculated as LS/OR. Females from all generations had a second postmortem measurement of OR and OD; furthermore, females from the 1st to the 5th generation had a second postmortem measurement of IE, RIE, LIE, ID, and ES.

A total of 3,031 and 1,477 records from 900 females were used to analyze LS and OR, respectively, whereas 1,081 records were used to analyze IE and ES. A total of 1,471 records were used for OD; 1,079 for ID, RIE, and LIE; and 770 for FS and PS. The number of animals in the pedigree was 1,107.

Statistical Analyses

Bayesian inference was used. Data augmentation was carried out to fill the data vector and have the same design matrices for all traits. Augmented data were not used for inferences, but permitted to simplify computing (Sorensen and Gianola, 2002). Bivariate and trivariate repeatability animal models were fitted to estimate genetic parameters and genetic trends. Ovulation rate was included in each analysis, both bivariates and trivariates. Correlations with OR were estimated using bivariate models. Trivariate analyses were used to estimate genetic parameters between traits different from OR.

The model assumed that OR, OD, LS, IE, RIE, LIE, ID, and ES were

$$y_{ijklmn} = YS_i + L_j + P_k + a_l + p_m + e_{ijklmn},$$

where YS_i is the effect of year-season (1 yr season every 3 mo: 32 levels for LS; 31 levels for OR and OD; 30 levels for IE, RIE, LIE, ID, and ES), L_j is the effect of lactation state of the doe (2 levels: 1 for lactating and 2 for not lactating does when mated), P_k is the effect of parity (5 levels for LS, 4 levels for the other traits), a_l is the additive value of the animal, p_m is the permanent environmental effect, and e_{ijklmn} is the residual of the model. The model for FS and PS did not include the parity effect or the permanent environmental effect because records came only from the second parity, and the year-season effect had 30 levels.

For the bivariate repeatability model, the traits were assumed to be conditionally normally distributed as follows:

$$\begin{bmatrix}\mathbf{y}_1\\ \mathbf{y}_2\end{bmatrix}\left|\mathbf{b}_1,\mathbf{b}_2,\mathbf{a}_1,\mathbf{a}_2,\mathbf{p}_1,\mathbf{p}_2,\mathbf{R}\right. \sim N\left(\mathbf{X}\begin{bmatrix}\mathbf{b}_1\\ \mathbf{b}_2\end{bmatrix}+\mathbf{Z}\begin{bmatrix}\mathbf{a}_1\\ \mathbf{a}_2\end{bmatrix}+\mathbf{W}\begin{bmatrix}\mathbf{p}_1\\ \mathbf{p}_2\end{bmatrix},\mathbf{R}\right),$$

where $\mathbf{b}_1$ and $\mathbf{b}_2$ were random vectors including the effects of YS, L, and P; $\mathbf{a}_1$ and $\mathbf{a}_2$ were vectors of individual additive genetic effects; and $\mathbf{p}_1$ and $\mathbf{p}_2$ were vectors of permanent environmental effects. The $\mathbf{X}$, $\mathbf{Z}$, and $\mathbf{W}$ were known incidence matrices; $\mathbf{R}$ was the residual (co)variance matrix. Between individuals, only the additive random effects were assumed correlated. Within individuals and between traits, the additive, permanent environmental, and residual effects were assumed correlated. The residual (co)variance matrix can be written as $\mathbf{R}_0 \otimes \mathbf{I}_n$, with $\mathbf{R}_0$ being the 2 × 2 residual (co) variance matrix between the traits analyzed and $\mathbf{I}_n$ an identity matrix of appropriate order. Bounded uniform priors were used to represent vague previous knowledge

Table 1. Means and SD for number of implanted embryos (IE), number of IE on the right and on the left uterine horn (RIE and LIE, respectively), implantatory difference [ID = (RIE – LIE)], embryonic survival (ES), fetal survival (FS), and prenatal survival (PS) in the base generation

Trait	IE	RIE	LIE	ID	ES	FS	PS
Mean	12.51	6.62	5.92	3.21	0.82	0.73	0.59
SD	3.17	2.64	2.48	2.48	0.18	0.19	0.2

of distributions of $\mathbf{b}_1$ and $\mathbf{b}_2$. Prior knowledge concerning additive and permanent effects was represented by assuming that they were normally distributed, conditionally on the associated (co)variance components, as follows:

$$\begin{bmatrix}\mathbf{a}_1\\ \mathbf{a}_2\end{bmatrix}\Big|\mathbf{G} \sim N\left(\mathbf{0},\mathbf{G}\right);$$

$$\begin{bmatrix}\mathbf{p}_1\\ \mathbf{p}_2\end{bmatrix}\Big|\mathbf{P} \sim N\left(\mathbf{0},\mathbf{P}\right),$$

where $\mathbf{0}$ was a vector of zeroes, $\mathbf{G}$ was the genetic (co)variance matrix, and $\mathbf{P}$ was the (co)variance matrix of the nonadditive genetic plus permanent environmental effects of the doe. Matrices $\mathbf{G}$ and $\mathbf{P}$ could be written as $\mathbf{G}_0 \otimes \mathbf{A}$ and $\mathbf{P}_0 \otimes \mathbf{I}_s$, respectively, where $\mathbf{G}_0$ and $\mathbf{P}_0$ were the 2 × 2 genetic and permanent (co)variance matrices, $\mathbf{A}$ was the known additive genetic relationship matrix, and $\mathbf{I}_s$ was the identity matrix of the same order as the number of levels of permanent effects. Bounded uniform priors were used for matrices $\mathbf{R}_0$, $\mathbf{G}_0$, and $\mathbf{P}_0$. For trivariate repeatability analyses, the order of the $\mathbf{R}$, $\mathbf{G}$, and $\mathbf{P}$ matrices was 3 × 3.

Marginal posterior distributions of all unknowns were estimated using the Gibbs sampling algorithm. The programs TM by Legarra et al. (2008) and GIBBS2F90 by Misztal et al. (2002) were used for all Gibbs sampling procedures. Chains of 1,000,000 samples each were used, with a burning period of 200,000. One sample each 50 was saved to avoid high correlations between consecutive samples. Convergence was tested using the Z criterion of Geweke.

RESULTS AND DISCUSSION

Means and SD of the traits IE, RIE, LIE, ID, and survival rates in the base generation are presented in Table 1; values of IE and survival rates are in agreement with values published by other authors in maternal rabbit lines (Brun et al., 1992; García and Baselga, 2002). Means and SD for OR, OD, and LS can be found in Laborda et al. (2011). In our experiment, prenatal mortality (1 − PS) expressed as a percentage was approximately 40% in the base generation, in agreement with results previously reported in rabbits (Adams, 1959, 1960), 18% corresponding to the embryonic period (preimplantation), and 22% to the fetal period (postimplantation). In pigs, a prenatal loss of 40 to 60% has been reported (reviewed by Foxcroft et al., 2006); most of it has been observed before d 30 to 35 of gestation. Prenatal mortality in mice is around 20% (Bradford, 1969; Clutter et al., 1990). This percentage is almost equally distributed between the pre- and the postimplantation period (reviewed by Wilmut et al., 1986).

In our experiment, we have differentiated between pre- and postimplantation mortality (1 – ES and 1 – FS, respectively). This difference was not applied in most selection experiments involving ovulation rate in pigs and mice. Thus, comparisons with our data have to be taken with caution. In pigs, fetuses cannot be individualized by observation of its external surface by laparoscopy; therefore, the number of fetuses was counted in vivo by laparotomy at d 50, which in this species corresponds to the middle gestation, reducing fetal survival and litter size (Neal et al., 1989; Johnson et al., 1999). In mice, the number of fetuses was measured after slaughtering the female near the end of gestation (d 17; Clutter et al., 1990) or at d 7 to 8 and d 16 of gestation (Bradford, 1969).

The features of the marginal posterior distributions of the heritabilities of IE, RIE, LIE, ID, and survival rates and the repeatabilities of IE, RIE, LIE, ID, and ES are shown in Table 2. Heritabilities of OR (0.16; $HPD_{95\%}$ [0.07, 0.25]), OD (0.03; $HPD_{95\%}$ [0.00, 0.07]), and LS (0.09; $HPD_{95\%}$ [0.03, 0.14]) were presented in Laborda et al. (2011). Their repeatabilities were 0.25 ($HPD_{95\%}$ [0.17, 0.32]), 0.09 ($HPD_{95\%}$ [0.03, 0.15]), and 0.19 ($HPD_{95\%}$ [0.15, 0.23]), respectively. Tables 3 and 4 present the features of the marginal posterior distributions of the phenotypic correlations between traits, and Tables 5 and 6 present the features of the marginal posterior distributions of the genetic correlations between traits. In general, genetic correlations were estimated with low accuracy, and often it was only possible to draw conclusions about their sign.

Number of IE

The IE had a low heritability (Table 2). This was of the same magnitude as the heritability of IE in rabbits (Bolet et al., 1994; Argente et al., 2000) and the heritabilities of the number of fetuses at different moments of gestation in rabbits (d 12), pigs (d 50), and mice (d 17; Blasco et al., 1993b; Johnson et al., 1999; Clutter et al., 1990, respectively). The estimated phenotypic correla-

Table 2. Features of the marginal posterior distributions of the heritability (h^2) and the repeatability (r) of number of implanted embryos (IE), number of IE on the right and on the left uterine horn (RIE and LIE, respectively), implantatory difference [ID = (RIE – LIE)], and embryonic survival (ES) and the heritability of fetal survival (FS) and prenatal survival (PS)[1]

Trait	h^2	$HPD_{95\%}$ (h^2)	$P_{0.10}$	k	r	$HPD_{95\%}$ (r)
IE	0.11	0.04, 0.19	0.58	0.05	0.22	0.13, 0.31
RIE	0.08	0.01, 0.14	0.24	0.03	0.22	0.11, 0.31
LIE	0.06	0.01, 0.13	0.13	0.02	0.14	0.05, 0.23
ID	0.03	0.00, 0.08	0.01	0.01	0.12	0.05, 0.20
ES	0.09	0.02, 0.17	0.39	0.04	0.20	0.11, 0.29
FS	0.24	0.10, 0.38	0.98	0.13	—	—
PS	0.14	0.04, 0.25	0.75	0.06	—	—

[1]$HPD_{95\%}$: high posterior density interval at 95%; $P_{0.10}$: probability of the heritability being greater than 0.10; k: limit for the interval [k, +1) of the heritability, having a probability of 95%.

tion of IE with OR (Table 3) had similar magnitude and sign compared with the ones obtained in these species. The posterior mean of the genetic correlation between IE and OR had a large $HPD_{95\%}$ interval (Table 5), but it was positive with a high probability ($P = 0.99$). Our result is in accordance with the ones obtained in pigs and mice, where a positive genetic correlation between IE and OR was estimated: 0.44 in pigs (Johnson et al., 1999) and 0.81 in mice (Clutter et al., 1990). Both estimates were also imprecise. The repeatability estimate of IE was 0.22 with $HPD_{95\%}$ [0.13, 0.31] (Table 2). This repeatability estimate leads to an estimated ratio of the permanent environmental variance to the phenotypic variance ($\mathbf{p^2}$) of 0.11. No repeatability or p^2 estimates of the traits IE, ID, or ES have been found in the literature. However, our estimate of p^2 is within the range reported in the literature for LS in rabbits (reviewed by Garreau et al., 2004).

Estimated phenotypic and genetic correlations between LS and IE were 0.57 (Table 4) and 0.46 (Table 6). Their probabilities of being positive were 100 and 98%, respectively. Similar phenotypic correlations but apparently greater genetic correlations were obtained in rabbits and pigs, possibly because the number of fetuses was measured at a later point of gestation (Blasco et al., 1993b in rabbits; Johnson et al., 1999 in pigs) or because genetic correlations were estimated with low accuracy.

Taken all together, IE is not a good candidate to improve LS by indirect selection, due to its low heritability (Table 2) and its moderately low genetic correlation with LS (Table 6).

The number of right and left implanted embryos had low heritabilities (0.08 and 0.06 for RIE and LIE, respectively; Table 2), in accordance with the ones obtained by Blasco et al. (1993b). In mice, different results were obtained: Clutter et al. (1990) showed different heritability estimates for the number of fetuses in the right and the left uterine horns at d 17 of gestation, being greater for the right side than for the left side (0.18 and 0.03, respectively). In our study, the phenotypic and the genetic correlations of OR with RIE and LIE were positive with a high probability ($P \geq 87\%$; Tables

Table 3. Features of the marginal posterior distributions of the phenotypic correlation between the traits analyzed: ovulation rate (OR), ovulatory difference (OD), number of implanted embryos (IE), number of IE on the right and on the left uterine horn (RIE and LIE, respectively), implantatory difference [ID = (RIE – LIE)], embryonic survival (ES), fetal survival (FS), and prenatal survival (PS)[1]

Trait	Mean	$HPD_{95\%}$	P	k
IE, OR	0.38	0.29, 0.47	1.00^a	0.30^a
RIE, OR	0.28	0.19, 0.38	1.00^a	0.20^a
LIE, OR	0.30	0.20, 0.38	1.00^a	0.22^a
ID, OR	0.00	−0.08, 0.09	0.55^a	-0.07^a
ES, OR	−0.07	−0.17, 0.03	0.92^b	-0.15^b
FS, OR	−0.26	−0.33, −0.19	1.00^b	-0.20^b
PS, OR	−0.28	−0.35, −0.21	1.00^b	-0.22^b
ID, OD	0.59	0.51, 0.65	1.00^a	0.53^a
RIE, LIE	−0.04	−0.12, 0.04	0.83^b	0.03^b

[1]$HPD_{95\%}$: high posterior density interval at 95%; P: probability of the phenotypic correlation being [a]greater than zero, [b]less than zero; k: limit for the interval [a][k, +1), [b](−1, k], having a probability of 95%.

Table 4. Features of the marginal posterior distributions of the phenotypic correlation between the traits analyzed: litter size (LS), number of implanted embryos (IE), implantatory difference [ID = (RIE – LIE)], embryonic survival (ES), fetal survival (FS), and prenatal survival (PS)[1]

Trait	Mean	$HPD_{95\%}$	P	k
IE, LS	0.57	0.51, 0.62	1.00^a	0.52^a
ID, LS	0.00	−0.09, 0.09	0.53^a	-0.08^a
ES, LS	0.52	0.47, 0.59	1.00^a	0.48^a
FS, LS	0.56	0.52, 0.60	1.00^a	0.53^a
PS, LS	0.89	0.88, 0.90	1.00^a	0.88^a
ID, PS	−0.06	−0.13, 0.02	0.93^b	0.00^b
ES, FS	−0.07	−0.15, 0.01	0.96^b	0.00^b

[1]$HPD_{95\%}$: high posterior density interval at 95%; P: probability of the phenotypic correlation being [a]greater than zero, [b]less than zero; k: limit for the interval [a][k, +1), [b](−1, k], having a probability of 95%; RIE and LIE: number of IE on the right and on the left uterine horn, respectively.

Table 5. Features of the marginal posterior distributions of the genetic correlation between the traits analyzed: ovulation rate (OR), number of implanted embryos (IE), number of IE on the right and on the left uterine horn (RIE and LIE), implantatory difference [ID = (RIE – LIE)], embryonic survival (ES), fetal survival (FS), and prenatal survival (PS)[1]

Trait	Mean	$HPD_{95\%}$	*P*	k
IE, OR	0.58	0.16, 0.93	0.99[a]	0.20[a]
RIE, OR	0.74	0.33, 1.00	0.99[a]	0.33[a]
LIE, OR	0.41	−0.29, 1.00	0.87[a]	−0.29[a]
ID, OR	0.56	−0.17, 1.00	0.91[a]	−0.17[a]
ES, OR	0.02	−0.57, 0.64	0.53[b]	−0.49[b]
FS, OR	−0.58	−1.00, −0.26	1.00[b]	−0.26[b]
PS, OR	−0.55	−1.00, −0.11	0.98[b]	−0.11[b]
ID, OD	0.69	−0.33, 1.00	0.92[a]	−0.33[a]
RIE, LIE	0.44	−0.03, 0.89	0.96[a]	0.01[a]

[1]$HPD_{95\%}$: high posterior density interval at 95%; *P*: probability of the genetic correlation being [a]greater than zero, [b]less than zero; k: limit for the interval [a][k, +1), [b](−1, k], having a probability of 95%.

3 and 5), indicating that RIE and LIE tend to increase with selection for OR. The phenotypic correlation between RIE and LIE was very low (Table 3), whereas the genetic correlation was positive with a high probability ($P = 96\%$; Table 5). In mice, the estimate of the phenotypic correlation between fetuses in the right and left uterine horn was close to zero (−0.01), and no accurate estimate of the genetic correlation between them was found (Clutter et al., 1990).

Implantatory difference refers to uneven embryo distribution through both uterine horns, where one uterine horn remains less occupied than the other one. Implantatory difference had a heritability close to zero, having only a probability of 1% of being greater than 0.10 ($P_{0.10}$; Table 2). Because there is no embryo uterine transmigration in rabbits (Adams, 1959), ID may be associated to ovulatory difference (**OD**). The estimate of the phenotypic correlation between OD and ID was 0.59, having a probability of 95% of being at least 0.53 (Table 3). The genetic correlation was positive ($P = 0.92$; Table 5). These positive correlations suggest that OD and ID may increase together. Implantatory difference was phenotypically uncorrelated with OR (Table 3). However, the genetic correlation with OR was positive with a probability of 91% (Table 5), indicating that ID could increase with OR. These different phenotypic and genetic correlations are due to a negative permanent environmental correlation between OR and ID (−0.50; $HPD_{95\%}$ [−1.00, 0.29]). Implantatory difference was suggested by Laborda et al. (2011) to cause greater prenatal mortality in overcrowded uterine horns, contributing to the lacking correlated response in LS in rabbits selected for OR. However, this hypothesis could not be tested because the phenotypic correlations of ID with PS and LS were close to zero (Tables 4) and the genetic correlations were estimated with low accuracy (Table 6).

Survival Rates

Heritabilities were low for ES and PS (Table 2). Heritability of FS was moderate, with a 98% probability of being greater than 0.10 (Table 2). Heritability estimates were similar to the estimates presented by Blasco et al. (1993b) in rabbits. The heritability estimate of PS also agrees with the estimates in pigs (Rosendo et al., 2007) and mice (Clutter et al., 1990). Estimated phenotypic correlations between OR and survival rates were negative with a probability of at least 92% (Table 3); however, they were of low magnitude, especially the phenotypic correlation between OR and ES that had a probability near 100% of being in the interval from −0.20 to 0.20. The estimated genetic correlation between OR and ES was imprecise, and nothing can be said about its sign (Table 5). The estimated genetic correlation of OR with FS was negative, having a probability of 95% of being less than −0.26 (k, Table 5). The genetic correlation of OR with PS was also negative ($P = 98\%$; Table 5). In previous studies in rabbits and pigs, correlations between OR and PS ranged from −0.14 to −0.45 (Blasco et al., 1993b, in rabbits; Rosendo et al., 2007, in pigs). In mice, the genetic correlation between OR and survival at d 17 of gestation was low, but it was estimated with low accuracy (Clutter et al., 1990). Phenotypic and genetic correlations of OR with the components of PS, ES, and FS are scarce in the literature. Our results agree with the ones published previously in rabbits (Blasco et al., 1993b). In pigs, Neal et al. (1989) found a negative genetic correlation (−0.56), estimated with a large SE, between OR and survival at d 50 in a line selected for an index of these 2 traits during 5 generations. Johnson et al. (1999) obtained a high and negative genetic correlation (−0.86) in the same line of pigs after 11 generations of selection for the same index followed by 3 generations of selection for LS.

Table 6. Features of the marginal posterior distributions of the genetic correlation between the traits analyzed: litter size (LS), number of implanted embryos (IE), implantatory difference [ID = (RIE – LIE)], embryonic survival (ES), fetal survival (FS), and prenatal survival (PS)[1]

Trait	Mean	$HPD_{95\%}$	*P*	k
IE, LS	0.46	0.06, 0.78	0.98[a]	0.12[a]
ID, LS	0.05	−0.60, 0.69	0.57[a]	−0.53[a]
ES, LS	0.69	0.39, 0.94	1.00[a]	0.40[a]
FS, LS	0.65	0.39, 0.90	1.00[a]	0.41[a]
PS, LS	0.91	0.85, 0.97	1.00[a]	0.85[a]
ID, PS	−0.15	−0.86, 0.53	0.65[b]	0.49[b]
ES, FS	0.02	−0.55, 0.59	0.53[a]	−0.46[a]

[1]$HPD_{95\%}$: high posterior density interval at 95%; *P*: probability of the genetic correlation being [a]greater than zero, [b]less than zero; k: limit for the interval [a][k, +1), [b](−1, k], having a probability of 95%; RIE and LIE: number of IE on the right and on the left uterine horn, respectively.

Litter size was positively correlated with ES, FS, and PS, having phenotypic and genetic correlations of similar magnitude (Tables 4 and 6). Genetic correlations were moderate with ES and FS and greater with PS, which had a 95% probability of being at least 0.85. The genetic correlation of LS with ES and FS had probabilities of 89 and 91%, respectively, of being greater than 0.5. The positive correlations between LS and survival rates agree with the estimates found in the literature (Blasco et al., 1993a, for a review; Blasco et al., 1993b, in rabbits; Johnson et al., 1999, and Rosendo et al., 2007, in pigs).

The moderate heritability of FS, together with its positive and moderately high genetic correlation with LS, convert FS into an interesting trait to select for in rabbits, being a better candidate than OR. No selection experiment for FS has been found in the literature. In rabbits, there is 1 experiment of selection for the number of dead fetuses from implantation until birth in unilateral ovariectomized females (Bolet et al., 1994). This trait had a very low heritability and variability, and no correlated response in LS was observed.

Response to Selection

The response to selection for OR (1.32 ova in 10 generations) and the correlated responses in OD (0.29 ova in 10 generations) and in LS (−0.15 kits in 10 generations) were already presented in a previous paper (Laborda et al., 2011). The correlated responses in IE, RIE, LIE, ID, and survival rates are shown in Figures 1 and 2. After 10 generations of selection, the correlated response in IE was 0.90 embryos, most of it taking place in the right side (0.76 embryos). The reduced response in ID (0.14 embryos), less than 0.5% per generation, was apparently not responsible for the lacking correlated response in LS (Laborda et al., 2011). Moreover, the small increase in ID seems to be due to a scale effect related to the increase in IE, similar to what happens with OD (Laborda et al., 2011). This was confirmed after analyzing ID fitting IE as a covariate, where no response to selection was observed (−0.036 in 10 generations).

To our knowledge, this is the first experiment of selection for ovulation rate where the responses in the 2 components of prenatal survival have been studied in the same animal because in pigs and mice, fetuses cannot be easily counted in vivo without increasing their mortality. In our experiment, PS decreased 0.065 in 10 generations, around 1% per generation. Leymaster and Christenson (2000) obtained a similar response in a line of pigs selected for ovulation rate for 11 generations. We did not observe any response in ES, but FS decreased 0.078 in 10 generations, around 1% per generation. Thus, this decrease in FS was responsible for the lack of correlated response observed in LS. As in this experiment, Freking et al. (2007) did not observe any changes in embryonic survival in unilateral hysterectomy-ovariectomy females in the line of pigs described by

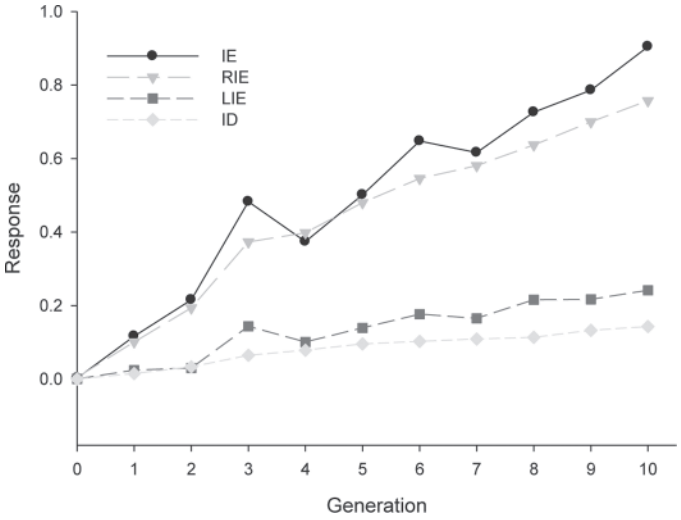

Figure 1. Genetic trends for number of implanted embryos (IE), right and left IE (RIE and LIE), and implantatory difference [ID = (RIE – LIE)]. Unit = embryos.

Leymaster and Christenson (2000); the main changes were observed during the early fetal development between d 25 and 45 of gestation associated to less endometrial space for the fetuses at implantation in the overcrowded uterine horns. Similarly, Bradford (1969) observed that postimplantation losses were the main cause for the uncorrelated response in litter size in the line selected for ovulation rate by comparing it with a control line and a line selected for litter size.

Most prenatal mortality in rabbits selected for OR occurred during the fetal period. A critical moment for fetal survival in rabbits is between d 8 and 17 of gestation, when the development of the placenta takes place (Adams, 1959, 1960; Hafez and Tsutsumi, 1966). Placental development in rabbits, as in mice, has been associated with the number of blood vessels at the implantation site (Duncan, 1969; Argente et al., 2003; Mocé et al., 2004, in rabbits; and Wirth-Dzieciolowska,

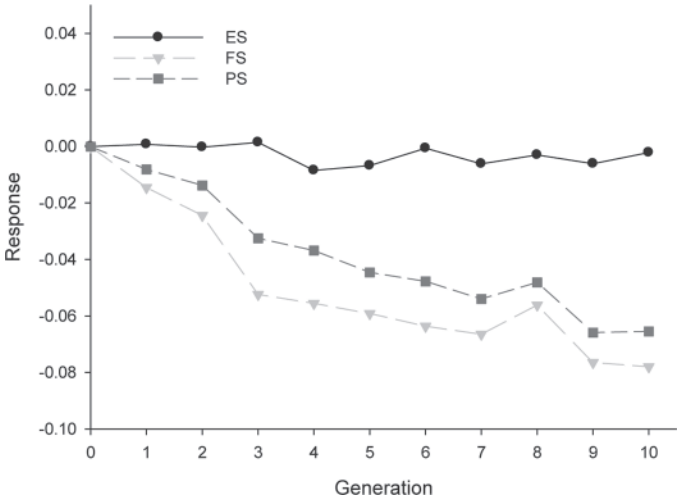

Figure 2. Genetic trends for embryonic survival (ES), fetal survival (FS), and prenatal survival (PS).

1987, in mice). Fetuses and fetal placentas are more developed when they receive more blood vessels, whereas fetuses with poor blood supply have a greater probability to die. In females with extremely high OR and overcrowded uterine horns, the blood flow to each fetus could be reduced, decreasing their survival.

Other explanations for the decreased FS could be immature oocytes or less developed embryos, which would not be able to survive in later states of gestation. The proportion of females with extremely high OR (more than 20 ova; i.e., twice the SD of the mean) increased with selection from 4 to 23%. These females could ovulate immature oocytes. A greater proportion of immature ova in pig females selected for OR compared with females from a control line was found by Koenig et al. (1986), who suggested that prenatal mortality could increase due to this, either before or after implantation. On the other hand, because follicles ovulate sequentially (Fujimoto et al., 1974), in females with high OR the ovulatory process could take longer than usual. A long ovulatory duration could lead to an increased variability in embryonic development (Torres et al., 1984). In rabbits, pigs, and mice, it was observed that the uterine environment was synchronic with the more developed embryos, which had a better chance to survive (Torres et al., 1984, in rabbits; Pope, 1988 and Xie et al., 1990, in pigs; Wilmut et al., 1986, and al-Shorepy et al., 1992, in mice). Less developed embryos have been related to reduced ES and FS in rabbits (Mocé et al., 2004; Peiró et al., 2007). In pigs, it has been demonstrated that less developed embryos were able to survive beyond implantation (Wilde et al., 1988; Pope et al., 1990); however, they would probably die soon after that due to fetal competence for space, contributing to the decrease in fetal survival (Geisert and Schmitt, 2002).

In conclusion, the results show that selection for OR has increased fetal mortality, whereas embryo mortality does not seem to have been modified. This fetal mortality has been the main cause for the lacking correlated response observed in LS. Some possible explanations would be a decreased blood flow arriving to each fetus or even immature oocytes or less developed embryos that die after implantation. Further studies are needed to explain the mechanism that has caused fetal mortality in rabbits selected for high ovulation rate.

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