

## Direct and correlated selection response for litter size and litter weight at birth in the first parity in mice

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Accepted 10 September 1997

### Abstract

Two lines of mice derived from the same base population were selected for seven generations. Line *S* was selected to increase litter size at birth and line *W* was selected to increase litter weight at birth. Two replicates were made in each line. Both traits were measured at first parity and litters were not standardized. Direct and correlated response were evaluated for both traits. Expected selection response and genetic gain were evaluated at the first and seventh generation of selection. No significant differences were found between expected selection responses and estimated genetic gain. The genetic gain estimated was significantly higher ( $p < 0.01$ ) for line *W* than line *S* for both traits. © 1998 Elsevier Science B.V.

*Keywords:* Selection; Mice; Litter size; Litter weight

### 1. Introduction

Genetic improvement of prolificacy traits in species such as pigs, rabbits and mink has considerable economic importance for total productivity. Litter size, one of the principal components of fitness, has a low heritability so that response from artificial selection is expected to be low (Eisen and Durrant, 1980). Genetic improvement in litter size at birth by selection in pigs is considered to be difficult because of its low heritability and low selection intensity due to the sex-limited nature of the trait (Rutledge, 1980; Vangen, 1981; Ollivier, 1982). Also, selection experiments for this trait have had little success in rabbits

(Rochambeau, 1988) or pigs (Haley et al., 1988). However, selection for litter size in mice has been more successful, with realized heritabilities between 0.05 and 0.20 (Eisen, 1978), especially when the first three parities were considered (Bayón et al., 1988).

An increase of litter size at first parity has been reported in mice as a correlated response of selection for growth (Hanrahan and Eisen, 1974), however, Von Butler et al. (1984) pointed out that litter size was significantly reduced as a result of inbreeding in lines selected for high body weight (reviewed by Brien, 1986).

Genetic correlation between litter size and litter weight reported by Luxford et al. (1990) was 1.0. Genetic correlations found between litter size and female body weight were 0.59 and 0.54 reported by Joakimsen and Baker (1977) and Eisen (1978) re-

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Table 1  
Parameter estimates of the base population

| Parameter              | Trait       |                            |
|------------------------|-------------|----------------------------|
|                        | Litter size | Litter weight <sup>a</sup> |
| Mean                   | 7.48 ± 0.12 | 10.23 ± 0.15               |
| Phenotypic Variance    | 5.22        | 8.03                       |
| Heritability           | 0.08        | 0.21                       |
| C-squared <sup>b</sup> | 0.16        | 0.14                       |
| Correlation            |             |                            |
| Phenotypic             | 0.96        |                            |
| Genetic                | 1.00        |                            |

<sup>a</sup>In grams (g).

<sup>b</sup>Common litter effect.

spectively. Although the genetic correlation between litter size and litter weight is found to be higher than the genetic correlation found between litter size and female body weight, only a few experiments have used litter weight as selection criterion (Eisen et al., 1970; Schüler, 1985, 1987; Luxford et al., 1990; Luxford and Beilharz, 1990; Gama and Johnson, 1992).

A possible way to increase litter size might be to select for litter weight at birth. The higher heritability of litter weight relative to litter size and the high genetic correlation between both traits suggest selection for litter weight at birth as an alternative method to improve litter size at birth.

## 2. Material and methods

The base population of mice used in this study was a three-way cross of inbred lines: BALB/c, CBA and C57BL. The three lines contributed equally to the three-way cross. After three generations of

panmixia, 347 litters were evaluated in the base population. Then, the population was split at random into two lines: one selected for large litter size at first parity (*S*) and one selected for large litter weight at first parity (*W*). There were two replicates for both lines *S* and *W*. Generations were discrete and lines were contemporary and at the same environmental conditions. In each line and replicate, 48 females were mated at random, each of them with one male avoiding full and half-sib matings, and were evaluated for both traits (litter size and litter weight at birth, defined as the number or the weight of all young born alive and dead) per generation, and 12 females with the largest litter size in lines *S* and largest litter weight in lines *W* were selected. Each selected female contributed four daughters and four sons to the next generation. Thus, four daughters per selected female were evaluated in the following generation. Cages were checked and litters weighed once daily. Selection was carried out during seven generations.

Mice were mated between nine and eleven weeks of age and the males were removed from the females 13 days after mating. The young were weaned at three weeks of age and placed in plastic cages separately by sexes, with four to six mice in each cage.

Throughout the experiment, the mice were maintained under laboratory conditions. The temperature in the mouse room ranged from 20°C to 24°C. A commercial pellet feed and tap water were supplied ad libitum.

Heritabilities and genetic and phenotypic correlations for the two traits were obtained by a derivative-free multivariate REML procedure (Smith and Graser, 1986), using the DFREML program written by Meyer (1991). This procedure has been used by

Table 2  
Phenotypic means for litter size per generation and line pooled across replicates

| Line     | Generations |             |             |             |             |             |             |             |  |
|----------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|--|
|          | G0          | G1          | G2          | G3          | G4          | G5          | G6          | G7          |  |
| <i>S</i> | 7.48 ± 0.12 | 8.62 ± 0.27 | 8.45 ± 0.21 | 9.07 ± 0.18 | 8.94 ± 0.23 | 8.12 ± 0.27 | 9.47 ± 0.26 | 9.39 ± 0.25 |  |
| <i>W</i> | 7.48 ± 0.12 | 8.72 ± 0.28 | 8.22 ± 0.25 | 8.47 ± 0.25 | 8.94 ± 0.24 | 8.41 ± 0.26 | 8.96 ± 0.29 | 9.12 ± 0.32 |  |

*S* selected line for litter size.

*W* selected line for litter weight.

Table 3  
Phenotypic means for litter weight (g) per generation and line pooled across replicates

| Line | Generations  |              |              |              |              |              |              |              |
|------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|
|      | G0           | G1           | G2           | G3           | G4           | G5           | G6           | G7           |
| S    | 10.23 ± 0.15 | 11.79 ± 0.36 | 12.35 ± 0.35 | 12.71 ± 0.24 | 12.78 ± 0.31 | 11.67 ± 0.39 | 13.34 ± 0.34 | 13.42 ± 0.33 |
| W    | 10.23 ± 0.15 | 11.96 ± 0.33 | 12.16 ± 0.37 | 12.28 ± 0.31 | 13.07 ± 0.33 | 12.47 ± 0.35 | 13.48 ± 0.39 | 13.87 ± 0.44 |

S selected line for litter size.  
W selected line for litter weight.

Meyer and Hill (1991) in a selection experiment in mice. The multivariate model was:

$$y = Xb + Zu + Wc + e \tag{1}$$

with:

$$\begin{bmatrix} y \\ u \\ c \\ e \end{bmatrix} \sim N \left[ \begin{bmatrix} Xb \\ 0 \\ 0 \\ 0 \end{bmatrix}, \begin{bmatrix} V & ZG & WP & R \\ (ZG)' & G & 0 & 0 \\ (WP)' & 0 & P & 0 \\ R & 0 & 0 & R \end{bmatrix} \right]$$

$$V = ZGZ' + WPW' + R$$

$$R = I_c \otimes R_0$$

$$G = A \otimes G_0$$

$$P = I_c \otimes P_0$$

where: **y** vector of observations, **X** incidence matrix of fixed effects, **Z** incidence matrix of animal effect, **W** incidence matrix of litter effect, **b** vector of unknown parameters for fixed effect, **u** vector of unknown parameters for animal, **c** vector of unknown parameters for litter, **e** vector of residuals, **I<sub>c</sub>** identity matrix of order equal to the number of records, **I<sub>l</sub>** identity matrix of order equal to the number of litters, **A** relationship matrix of order number of animals, **R<sub>0</sub>** residual covariance matrix among measurements on the same animal, **G<sub>0</sub>** covariance matrix for additive genetic effects, **P<sub>0</sub>** covariance matrix for litter effects and  $\otimes$  Kronecker product.

The REML values do not include the standard errors because the procedure used is a iterative method.

The expected direct and correlated responses in the first generation of selection were estimated (Falconer, 1983) as:

$$DR_1 = i h_1^2 \sigma_{p1}$$

$$CR_2 = i h_1 h_2 r_g \sigma_{p2}$$

where: **DR<sub>1</sub>** direct response of trait 1, **CR<sub>2</sub>** correlated response of trait 2, *i* selection intensity,  $h_1^2$  heritability for trait 1,  $h_2^2$  heritability for trait 2,  $\sigma_{p1}^2$  and  $\sigma_{p2}^2$  phenotypic variances and  $r_g$  genetic correlation.

The disequilibrium generated on the variance each generation along selection process are cumulative. For this reason, the parameters included in DR and CR must be re-calculated each generation. The expected direct and correlated responses at the seventh generation of selection were estimated, including the effect of the selection on the genetic variance (Bulmer, 1971, 1976; Tallis and Leppard, 1987) as:

$$G_{j+1} = 1/2G_j + 1/2G_0 - 1/2k(G_j b b' G_j) / P_{11}$$

The equation shows the change of genetic effects in one generation only, where: **G<sub>j</sub>** variances and covariances matrix of genetic effects on *j* generation, **P<sub>11</sub>** phenotypic variance of selected trait, *b* and *b'* incidence vectors and

$$k = i(i - x)$$

where: *i* intensity of selection and *x* deviation of the point of truncation.

The expected response standard error was estimated at first and seventh generations following Hill (1974).

Table 4  
Cumulated selection differential (*S<sub>c</sub>*), realized heritability ( $h_r^2$ ) and realized genetic correlation ( $r_g$ ) after seven generations of selection

| Trait                | Size | Weight |
|----------------------|------|--------|
| <i>S<sub>c</sub></i> | 5.73 | 7.56   |
| $h_r^2$              | 0.33 | 0.48   |
| $r_g$                | 0.87 |        |

Table 5  
Direct expected responses (ER) and genetic gain estimated (OR) after one and seven generations of selection

| Line | Trait  | 1st           |               | 7th           |               |
|------|--------|---------------|---------------|---------------|---------------|
|      |        | ER            | OR            | ER            | OR            |
| S    | Size   | 0.117 ± 0.253 | 0.115 ± 0.039 | 0.803 ± 0.362 | 0.979 ± 0.044 |
| W    | Weight | 0.373 ± 0.364 | 0.426 ± 0.062 | 2.491 ± 0.664 | 3.160 ± 0.085 |

S selected line for litter size.

W selected line for litter weight.

Table 6  
Correlated expected responses (ER) and genetic gain estimated (OR) after one and seven generations of selection

| Line | Trait  | 1st           |               | 7th           |               |
|------|--------|---------------|---------------|---------------|---------------|
|      |        | ER            | OR            | ER            | OR            |
| S    | Weight | 0.232 ± 0.343 | 0.228 ± 0.078 | 1.596 ± 0.580 | 1.946 ± 0.088 |
| W    | Size   | 0.187 ± 0.324 | 0.214 ± 0.031 | 1.253 ± 0.500 | 1.589 ± 0.042 |

S selected line for litter size.

W selected line for litter weight.

The realized heritability and the realized genetic correlation after seven generations of selection were calculated (Falconer, 1983) as:

$$h_r^2 = DR_c / S_c$$

$$r_g^2 = CR_1 CR_2 / DR_1 DR_2$$

where:  $h_r^2$  realized heritability,  $S_c$  accumulative selection differential and  $r_g^2$  realized genetic correlation.

The observed direct and correlated phenotypic selection response was obtained from phenotypic means pooled across replicates.

Genetic values were obtained by using the multi-trait animal model described in Eq. (1). Genetic trends in the selection process were obtained from regression of genetic values on generation number in which the animal was born.

The Student's *t*-test was used to compare all responses.

### 3. Results

The parameter estimates in the base population are shown in Table 1. Both traits have a similar coefficient of variation ( $\sigma/X$ ), 0.30 for litter size and 0.27 for litter weight and similar common litter effect ( $c^2$ ).

Tables 2 and 3 show the change of phenotypic means per generation for litter size and litter weight, respectively. In both tables, line noted S was selected for litter size and line noted W was selected for litter weight. The means in each replicate and generation were calculated from individual phenotypic values. In each selected line S and W means were pooled over replicates because no significant differences were found between replicates.

Table 4 shows cumulated selection differential, realized heritability and realized genetic correlation after seven generations of selection for litter size and litter weight. The cumulated selection differential and realized heritability were calculated in line S for litter size and in line W for litter weight.

Table 7  
Average genetic gain per generation

| Trait  | Line          |                   |
|--------|---------------|-------------------|
|        | S             | W                 |
| Size   | 0.140 ± 0.006 | 0.223 ± 0.005 * * |
| Weight | 0.278 ± 0.012 | 0.443 ± 0.011 * * |

S selected line for litter size.

W selected line for litter weight.

\* \*  $P < 0.01$ .

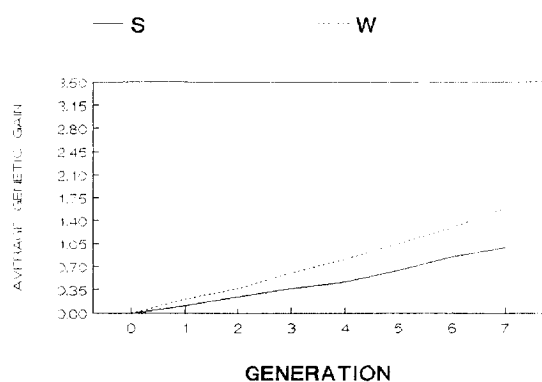


Fig. 1. Genetic trend for litter size (in pups).

The realized heritabilities were higher than the values estimated in the base population. The realized genetic correlation was lower than that estimated in the base population.

The comparison between expected and estimated selection responses for generations one and seven of selection is shown in Table 5 for direct response and in Table 6 for correlated response.

The genetic gain across selection process was estimated from regression of genetic values on generation number.

No significant differences were found between expected and estimated responses.

Table 7 shows the regression coefficients of genetic trends in lines W and S for both traits. Correlated response for litter size was significantly higher ( $p < 0.01$ ) than direct response. Direct response for litter weight was significantly higher ( $p < 0.01$ ) than the correlated response.

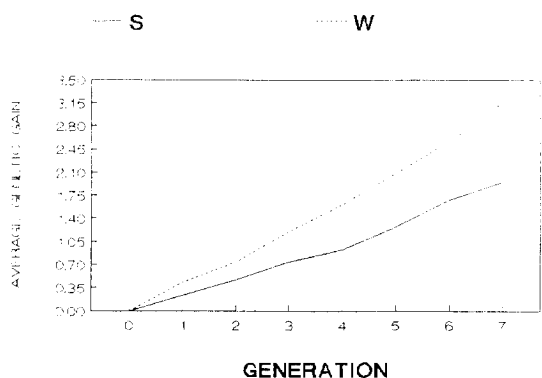


Fig. 2. Genetic trend for litter weight (in grams).

Figs. 1 and 2 show the average genetic gain across generations for litter size and litter weight, respectively. Line W has a higher result for both traits than line S.

#### 4. Discussion

The heritability estimates in the base population are low and agree with those for traits related with fitness.

The heritability of litter size at birth agrees with estimates previously reported by other authors in mice (Falconer, 1960; Luxford and Beilharz, 1990) and hamsters (Satoh and Nishida, 1990). However, the heritability estimates reported in many other cases are higher than those obtained in our experiment for this trait in mice (Eklund and Bradford, 1977; Eisen and Johnson, 1981; Schüler, 1987), pigs (Johanson, 1981), sheep (Hanrahan, 1982) or rabbits (Baselga et al., 1982).

Concerning litter weight at birth, the scarce amount of experiments in mice (Schüler, 1985, 1987) and pigs (Gama and Johnson, 1992) does not permit the establishment of comparisons with our data.

The values of common litter effect are consistent and similar for both traits. This effect was included in the multivariate model because the relationships between animals permit the separation of the common litter effect and the direct genetic effect. The common litter effect is corrected for average genetic litter effect.

The perfect genetic correlation found for litter size and litter weight at birth suggests the same genes are associated with both traits without antagonist effects involved. Nevertheless, the realized genetic correlation was slightly lower (Table 4).

Since litter weight is the product of mean individual body weight of the progeny and litter size of the mother, the high phenotypic and genetic correlation found for litter size and litter weight at birth also indicates a low variability of individual body weight at birth. In our case, the values for mean, phenotypic variance and genetic variance, for this trait, are respectively 1.39 g, 0.025 g and 0.0032 g in the base population.

A perfect genetic correlation has been reported for litter size and litter weight at birth in mice by Luxford et al. (1990) and for litter size and litter weight at weaning by Luxford and Beilharz (1990).

The expected selection correlated response in litter weight at weaning when selection criterion is litter size or mean individual weaning weight has been reported by Eisen (1981). In the case of individual selection, indirect selection for total litter weight at weaning using litter size is more efficient than using mean individual body weight when heritability for litter size is higher than heritability for mean individual body weight and the level of genetic correlation between litter size and individual body weight increases.

In our case, genetic correlation has been estimated between total litter weight and litter size at birth. It would be better to select for litter weight because its heritability is higher than the heritability of litter size and the direct and correlated expected response in the line *W* was higher than line *S* (Tables 5 and 6).

The realized heritability values (Table 4) calculated from phenotypic means (Tables 2 and 3) were higher than heritability estimated in the base population but, when genetic trends were considered no significant differences were found between observed and expected responses (Tables 5 and 6). Many experiments report the lack of good agreement between expected and observed selection responses as pointed out by Sheridan (1988). In mice, for litter size, Eklund and Bradford (1977) obtained a realized heritability higher than estimated in a control line derived from the base population. Fuente and San Primitivo (1985) report good agreement between estimated and realised parameters for litter size when the first three parities are considered.

When the selection response is studied in terms of genetic trend, the indirect selection for litter size was significantly higher than direct selection (Table 7, Fig. 1) and for litter weight direct selection was significantly higher than indirect selection (Table 7, Fig. 2). This results agree with the higher value of heritability for litter weight than for litter size and with the value of the genetic correlation.

Direct and correlated selection responses for these traits have been reported. Litter size at birth has resulted in positive correlated response in total litter weight at weaning (Eisen and Durrant, 1980). Direct

selection for total litter weight in standardized litters has yielded positive response (Eisen et al., 1970). Luxford and Beilharz (1990) obtained a higher selection response in mice to improve litter weight at weaning by direct selection rather than by selecting through litter size. Correlated response after eight generations of selection to increase litter size in swine, after previous selection for ovulation rate, were evaluated for litter weight at birth and weaning by Gama and Johnson (1992). They found an increase for litter size but no changes were observed for litter weight at birth. Schüller (1985) combined both litter size and litter weight as an index and concluded that the index was more effective than direct selection to increase litter size. Campo and Sánchez de la Blanca (1988) found a better response for biomass in *Tribolium*, using a quadratic selection index instead of using direct selection, and direct selection was still better than indirect selection through the family size trait.

The results obtained in our experiment indicate a higher genetic gain in line *W* than line *S* for both traits. So, an increase for an interesting trait in livestock production like litter weight at birth could be also an appropriate strategy to increase litter size.

### Acknowledgements

We thank the Dirección General de Ciencia y Tecnología for financial support and M. Toro and A. Blasco for their comments on this paper.

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