Estimation of parameters relating with canalisation of litter size and litter weight at birth in mice

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Summary

Genetic parameters of variability of litter size, and litter and mean individual weight at birth in mice, have been explored from a base population designed to conduct an experiment aiming to decrease genetic variability of litter size. The founder population of the future experiment consisted of 875 females daughters of 43 males with two consecutive parities in order to select males based on the phenotypic minimum litter size variability.

Genealogical data was traced back 18 generations being the litter size at birth the only trait recorded in animals found in historical pedigree. The whole data set consisted of 4129 records of litter size and 1796 of mean individual and total litter weight records considering up to 3997 pedigree records.
The methodology used in the treatment of data was that proposed by SanCristobal-Gaudy et al., 1998. Based on this, the logarithm of the squared of the estimated residuals resulting from a BLUP evaluation, were used to estimate variance components via REML.

The heritabilities of the variability under an univariate model were 0.0040, 0.0072 and 0.0139 for litter size, litter weight and mean individual weight at birth respectively. Heritabilities were slightly higher when bivariate models for mean and variability traits where analysed together. Genetic correlations between them were –1.00, -0.97 and 0.84 for litter size, litter weight and mean individual weight at birth. These results suggest a low genetic base for variability of the evaluated traits. A selection generation can be carried on in order to have an estimate of realized heritability.

Introduction

Over last years, selection prolificacy in prolific species like pigs and rabbits, has induced an increase in litter size. As a consequence, the ability of the young to survive has been reduced and the mortality rate during lactation has also increased. Several factors were identified to explain the phenomenon, like a lower birth weight within large litters or an unfavourable genetic relationships between litter size and survival rate. Peri- and postnatal survival rates are then related to birth weight, and more precisely to its heterogeneity. Thus, reducing the heterogeneity of birth weight should improve survival rate.

Modelisation of heterogeneity is not easy but it is based on the hypothesis of the existence of a pool of genes controlling the mean of the performance and another pool of genes controlling the homogeneity of the performance when environment is modified (Schneiner and Lyman, 1991).

SanCristobal-Gaudy *et al.* (1998) developed a method to deal with genetics of variability. Based on it, a first estimation of the heritability of the homogeneity has been obtained for birth weight in rabbits (Garreau et al., 2004).

Genetic of variability is, then, a rather new concept and, before setting up animal breeding programs, selection experiments with laboratory mammals are actually necessary. A better biological understanding of the genetics of variability is needed before to carry out any selection experiment.

In order to study genetic parameters related to birth weight variability in mammals, an experiment using mice have been designed and it is being carried out, since this specie is a good mammalian model for sheep, pigs and rabbits, with the advantage of a short generation interval.

Before conducting artificial selection it should be useful to ascertain the genetic parameters of the involved traits. The objective of this study was to estimate variance and covariance components of the litter size, litter birth weight and individual mean birth weight variability.

Material and Methods

The origin of the population of mice that was used in this study was a three-way crossed of inbred lines: Balb/c, C57BL and CBA that contributed equally to the base population. This population has been maintained during 20 generations of panmixia, which ensures a high genetic and phenotypic variability.

A mating plan was designed to have a fixed genetic background taking full advantage of the existence of inbred lines in mice. 43 males of the base population were mated to females of the Balb/c inbred line, to be evaluated through an original progeny test by simply computing the variance of the litter size of their daughters. A total of 875 females obtained of those progenies were newly mated with males of the Balb/c inbred line and evaluated for litter size, litter birth weight and individual mean birth weight at two consecutives parities.

A resulting data set of these matings is useful to compute genetic parameters. The inbred animals were considered as the same animal in the pedigree file and the rest of the genealogical data was traced back 18 generations. The whole data set consisted of 4129 records of litter size and 1796 of mean individual and total litter weight records considering up to 3997 pedigree records.

The three analysed traits were considered as traits of the mother in all the cases.

The methodology used in the treatment of data was the proposed by SanCristobal-Gaudy et al. (1998) and has been recently used in rabbits Garreau et al. (2004).

The analysis was performed in three steps:

1.- Firstly, the estimation of genetic parameters of the three traits via REML. The matricial notation of the sets of mixed model equations to be solved are $\mathbf{y} = \mathbf{Xb} + \mathbf{Zu} + \mathbf{Wp} + \mathbf{e}$, with:

$$\begin{pmatrix} y \\ u \\ p \\ e \end{pmatrix} \approx N\left(\begin{bmatrix} Xb \\ 0 \\ 0 \\ 0 \end{bmatrix}, \begin{bmatrix} V & ZG & WP & R \\ GZ' & G & 0 & 0 \\ PW' & 0 & P & 0 \\ R & 0 & 0 & R \end{bmatrix}\right)$$

where $\mathbf{V} = \mathbf{ZGZ'} + \mathbf{WPW'} + \mathbf{R}$, $\mathbf{G} = \mathbf{A}\sigma^2_u$, $\mathbf{P} = \mathbf{I_{ep}}\sigma^2_{ep}$, $\mathbf{R} = \mathbf{I_e}\sigma^2_e$, and **y** is the vector of observations, **X** the incidence matrix of fixed effects, **Z** the incidence matrix of animal effect, **W** the incidence matrix of permanent environmental effect, **b** the vector of unknown parameters for fixed effect, **u** the vector of unknown parameters for direct animal genetic effect, **p** the vector of unknown parameters for permanent environmental effect, **e** the vector of residuals, $\mathbf{I_e}$ the identity matrix of equal order to the number of records, $\mathbf{I_{ep}}$ the identity matrix of equal order to the number of females having litters, **A** is the numerator relationship matrix, σ^2_u the direct genetic variance, σ^2_{ep} the permanent environmental variance, and σ^2_e is the error variance.

The fixed effects of the model were the generation number (20 levels), and the light conditions effect with three levels: continuous light, continuous darkness or normal light conditions.

2.- This methodology assumes that the residual of the model can be decomposed into a part under genetic control and the usual unexplained variability. Thus, the second step consisted of solving the model, obtaining of a vector of residuals by $\mathbf{\hat{e}} = \mathbf{y} - \mathbf{Xb} - \mathbf{Zu} - \mathbf{Wp}$, and defining a new variable by transforming each value in the $\mathbf{\hat{e}}$ vector by $z_i = \ln(\hat{e}_i^2)$.

3.- Finally the new vector **z** was analysed to estimate genetic parameters following the model described above but leaving out the permanent environmental effect which is basically the conceptual trait analysed in this step. This last step was also carried out under a bivariate model together with the original trait to obtain genetic and phenotypic correlations between mean and variability of each trait.

All computations were carried out by using VCE program (Neumaier and Groeneveld, 1998), and by own programs when needed.

Results and discussion

Obtained genetic parameters under a univariate model, both for each trait and their variability, are shown in table I. Obtained results under a bivariate model are shown in table II.

The heritabilities both for the traits and for their variability under the bivariate model were slightly higher than when an univariate model was used. Genetic correlations between the trait and its variability were highly negative for litter size and litter birth weight but positive for individual mean birth weight.

These are the first estimates of heritability for variability of traits in mice. The highest heritability value for variability was obtained in the bivariate model for litter size but all of them where very similar and consistent with the value of 0.012 obtained for individual birth weight in rabbits (Garreau et al., 2004). Even though these values are dramatically lows, they may not be interpreted as normal heritability coefficients since transformation applied on the residuals lead to non linearity of the model.

The heritability for variability has been previously analysed for other authors working directly on the standard deviation of individual weights. So, for example, Damgaard et al. (2003) found the heritability for within-litter variation in piglet birth weight to be 0.08 ±0.03 and for weight at three weeks of age as 0.06±0.03. The heritability for weaning litter size variation reported by Huby et al. (2003) was 0.02 ± 0.01.

Present results and those from literature suggest a low genetic base for variability of the evaluated traits. Even so, genetic improvement of these traits by artificial selection should be possible since traits with low heritabilities like litter size had been successfully selected. A selection generation may be undertaken in order to have an estimate of realized heritability.

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Table I: Heritability for the direct genetic effect (h^2), environmental permanent variance as a proportion of phenotypic variance (c^2), repeatability (r), and heritability of the variability (h^2_v) for the three analysed traits using an univariate model.

Trait	**h^2**	**c^2**	**R**	**h^2_v**
LS	0.0990	0.0946	0.1936	0.0040
LW	0.1337	0.0599	0.1936	0.0072
IW	0.0298	0.0952	0.1249	0.0139

Table II: Heritability for the direct genetic effect (h^2), environmental permanent variance as a proportion of phenotypic variance (c^2), repeatability (r), heritability of the variability (h^2_v), and genetic (r_G) and phenotypic (r_P) correlations between the traits and their variability for the three analysed traits using a bivariate model.

Trait	**h^2**	**c^2**	**R**	**h^2_v**	**r_G**	**r_P**
LS	0.1087	0.0864	0.1951	0.0144	-1.0000	-0.1027
LW	0.1479	0.0507	0.1986	0.0136	-0.9705	-0.0117
IW	0.0327	0.0622	0.0949	0.0139	0.2589	0.8388