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Estimation of the Effect of Inbreeding and Selection using an Animal Model

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ABSTRACT. *An inbred strain of mice (IQS) has been created from highly fecund base population (QS), by 20 generations of full-sib mating combined with selection for high litter size and low inter-litter-interval. Given the complexities of estimation of dominance effects in analysing inbred data, a simple and more accurate method was preferred for the present analyses. Accordingly, repeated-records animals model was fitted incorporating the inbreeding coefficient of the animal as a fixed effect to disentangle and estimate the effect of simultaneous processes of inbreeding and selection. The inbreeding depression of reproductive traits were 0.14, 0.19 and 0.01 per 10% increase in inbreeding coefficient for litter size, inter-litter-interval and pups born per week, respectively. Two body weight traits showed varying effect with the change of inbreeding coefficient. The response to selection for litter size trait was 0.05 pups increase per generation.*

INTRODUCTION

Inbreeding and selection are two ways of changing the genetic constitution of a population. In literature, the beneficial effects of selection and the harmful effects of inbreeding have been discussed in detail. Inbreeding have been used intentionally in the formative stages of many breeds of livestock considering as a mean of genetic improvement (Falconer, 1989) However, many studies have shown conclusively that on average, inbreeding decrease performance, especially for traits associated with reproductive ability and viability (McNeil *et al.*, 1989 and Burrow, 1993).

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In modern animal production, artificial breeding methods are quite extensively used. Artificial Insemination (AI) enables extremely intensive use of an individual male. When used indiscriminately, AI increases the chances of mating relatives (Burrow, 1993). In these circumstances, a proper investigation of evaluation of the effects of inbreeding is necessary.

In evaluating the genetic influence of inbreeding, two effects have to be incorporated. One is the covariance between the breeding values of related parents. The other is inbreeding depression, which is the adverse effect of inbreeding on the performance of individuals. The former can be accounted for by including all animals in the numerator relationship matrix, and the latter by including the effect of inbreeding in the statistical model (Casanova *et al.*, 1992 and Vanraden, 1992).

Mixed model methodology has recently been developed to evaluate the effect of inbreeding. The genetic trend of the population is evaluated through the estimation of breeding values of animals in the population with Best Linear Unbiased Prediction (BLUP) in an animal model. BLUP, which was first developed by Henderson in 1949, makes use of all available information on all the individuals, including both their pedigrees and phenotypic values, and incorporates them into an index with appropriate weighting. It also has the capacity to handle fixed effects. The BLUP procedure requires a prior knowledge of the heritability. The analysis provides estimates of the mean and of the fixed effects, and predicted breeding values of all the animals (Falconer, 1989). The development by Henderson (1976) and Quass (1976) of a rapid method of computing the inverse of the numerator relationship matrix expanded the use of the BLUP procedure and enabled the use of the animal model in genetic evaluation in large population.

In the present study it was tried to use animal model to evaluate the genetic progress in inbred population. Since both inbreeding and selection response were to be estimated, inbreeding coefficient was incorporated in the animal model to facilitate the isolation of each estimate. Data for the study were generated by brother-sister inbreeding of highly prolific strain of mice.

MATERIALS AND METHODS

Animals

Inbred mice (IQS) were derived from a highly fecund strain of mice called Queckenbush Swiss (QS) by brother-sister mating for 20 generations

(98.6% inbred). During inbreeding IQS mice have been selected for large litter and low inter-litter-interval. Because of selection, more than one family have been kept in each generation. Selection was done within family as well as across families. According to this selection pattern, the families (made up of brother-sister sets) not fulfilling the criteria of selection were dropped and some families were expanded during inbreeding.

Data

Data were collected from each mating pair that existed in any generation until they produced two consecutive litters. Data were recorded from 792 animals on the characters listed below:

1. Litter size (LS) - the number of live pups born for the first two consecutive litters.

2. Inter-litter-interval - the time period between initial mating and birth of the first litter (ILI_1), and the time period between consecutive litters (ILI_2).

3. Pups produced per week (PPW) - the ratio between total number of pups born in two litters and number of days between the initial mating and the birth of the second litter.

4. Initial mating weight (IMW) - body weight just before initial mating (when 50 days old).

5. Post parturition weight (W) - body weight after each parturition.

The new born litters were recorded on each weekday. The data structure was described in Table 1. Full pedigree information was recorded for all individuals throughout the period of study.

Analyses

The analyses were conducted to investigate the effect of inbreeding with selection for high LS and low ILI. Accordingly, primary consideration was given for the analysis of reproductive performance. Body weight changes were the correlated response.

Table 1. **Data structure and heritabilities used* for reproductive and body weight traits of QS and IQS mice.**

Trait	QS Mean ± s.d.	IQS Mean ± s.d.	h^2
LS	16.7 ± 4.0	15.5 ± 3.5	0.19
ILI	24.1 ± 7.3	25.3 ± 6.6	0.12
PPW	6.6 ± 1.4	4.4 ± 1.1	0.28
IMW	32.2 ± 3.5	33.6 ± 3.7	0.46
W	52.0 ± 6.0	43.1 ± 8.0	0.28

* heritabilities were estimated in a different study for the QS population (Silva, 1994).

Calculation of inbreeding coefficient

The coefficient of inbreeding, derived by Wright (1922), was calculated for all the individuals in the data set. All available relationships among both males and females were used to calculate the inbreeding coefficient, using a computer programme (Tier, 1990).

Statistical model

The repeated-records animal model was fitted, including the inbreeding coefficient of the dam as a fixed effect. Even though the common way of evaluating the effect of inbreeding is regression of inbreeding coefficient on performance, it couldn't apply to the present study as it is because, the inbreeding effect has been apposed by the force of selection. Under this situation the regression analyses will be biased upward. In order to remove this biasness, two forces of inbreeding and selection should be separated and effects should be estimated separately. Therefore, inbreeding coefficient of the dam was fitted as a fixed effect with a complete pedigree. The model fitted (as given below) enabled best linear unbiased estimates of both inbreeding depression and genetic trend (selection effect given via estimated breeding values).

Model :

$$Y_{ijk} = \mu + I_i + P_j + a_k + e_{jk}$$

where

Y_{ijk} = phenotype of the kth female, recorded from the jth parity at the ith level of inbreeding
μ = overall mean
I_i = fixed effect of ith inbreeding level of dam
P_j = fixed effect of ith parity
a_k = breeding value of kth female
e_{jk} = residual

The inbreeding effect of the litter was not included in to the model since it is totally confounded with inbreeding level of dam under continuous inbreeding situation. Heritabilities used were given in Table 1.

The inbreeding depression was then estimated by weighted regression of the best linear unbiased estimates of the effects of inbreeding on level of inbreeding. The response to selection was estimates from the averaged estimated breeding values in each generation.

A general purpose package for multivariate prediction and estimates called PEST (Groenveld *et al.*, 1990) was used to solve BLUP equations, using a repeated-records animal model.

Environmental trend

The environmental trend was assessed by considering the QS population (the base population) which was maintained in the same mouse-house for the entire duration of 20 generations of full-sib mating of IQS. For this purpose, QS litter size data were obtained for the entire period, and average litter size (over the first two litters) was estimated for each month of that period. Environmental trend was then estimated as the regression of average litter size on month.

RESULTS AND DISCUSSION

Phenotypic information

Over the entire 20 generations, IQS had an average of 15.7 ± 0.6 pups born alive. The fertility of mice decreased initially as the level of inbreeding reaches 80-90% and thereafter increased. This initial increase of infertility may be due to the dramatic increase of level of inbreeding at the initial stage. The accompanying selection might have kept those families which were stable at high level of inbreeding. Therefore, the inbreeding effect has been reduced in later generations. After 20 generations, only 18.8% of matings failed to produce a litter. Therefore in general, the fertility of the inbred mice was quite high. The weighted regression (weighted on number) of percentage of females that had no litter (*i.e.* infertility) on their level of inbreeding showed an increase of 0.7% per 10% increase of inbreeding. This high level of fertility is a result of the combination of starting with high base (QS mice are highly fertile) and the application of within-line selection which helps to select against unfavourable alleles.

Environmental trend

The analyses of QS population over the time period corresponds to the total time period of 20 generations of inbreeding in the IQS population suggested that there was no change (P=0.628) in litter size over time. Therefore there is no reason to assume that a systematic deterioration or improvement of the environmental condition of the population occurred during the time period considered in this study.

Effect of breeding

Reproductive traits

The solutions of the repeated-records animal model produces estimates for the effect of inbreeding of dam. The results of these analyses are summarised in Table 2. The estimates of inbreeding depressions were 0.14 pups decrease, 0.19 days increase and 0.01 pups decrease per 10% increase in inbreeding coefficient for LS, ILI and PPW respectively. The estimate of the inbreeding depression of the LS was substantially lower compared to the estimates given in the literature where it ranged from 0.19 to 0.56 (Bowman

Table 2. **The effect of inbreeding of the dam on litter size (LS), inter-litter-interval (ILI), pups-per-week (PPW), initial mating weight (IMW) and post partum weights (W) of IQS mice.**

Theoretical level of inbreeding[1]	Generation	Trait				
		LS	ILI	PPW	IMW	W
0.000000	0	16.9	22.2	5.3	40.0	-
0.250000	1	16.1	21.1	5.0	35.2	-
0.375000	2	11.6	25.6	3.3	38.5	-
0.500000	3	16.4	23.3	4.7	35.9	-
0.593750	4	15.6	24.4	4.5	38.6	-
0.671875	5	16.4	26.2	4.5	35.7	48.5
0.734375	6	16.5	23.8	4.8	33.1	46.6
0.785156	7	15.5	25.0	4.3	34.1	45.9
0.826172	8	14.3	27.1	3.8	33.6	45.2
0.859375	9	16.2	25.1	4.5	33.6	44.1
0.886230	10	16.0	26.6	4.7	33.5	47.1
0.907959	11	16.4	25.1	4.7	33.0	47.9
0.925537	12	15.8	26.0	4.3	32.1	47.5
0.939758	13	16.6	26.4	4.7	32.5	48.1
0.951263	14	15.8	25.6	4.3	32.6	47.9
0.960571	15	16.0	25.4	4.4	31.9	47.8
0.968102	16	16.5	24.9	4.7	32.5	47.5
0.974194	17	15.5	24.3	4.5	32.8	48.5
0.979122	18	15.4	26.3	4.1	33.0	48.1
0.983109	19	15.5	23.9	4.6	32.8	48.9
0.986335	20	14.8	24.9	4.1	32.6	48.0
Inbreeding depression[2]		0.14	0.19	0.01		

1 level of inbreeding of the dam.
2 weighted linear regression of inbreeding effect on inbreeding level of the dam.

and Falconer, 1960; Eisen and Hanrahan, 1974; Beilharz, 1982; Brewer *et al.*, 1990). This may be due to two reasons. One is the extremely high litter size (on average 16.25 ± 0.22 pups born alive) of base population from which the IQS population was derived. The other reason is the strong within-line selection. The latter might have helped to avoid unfavourable alleles and then fix the favourable alleles in the population. No comparable estimates were found in the literature for ILI and PPW estimates.

Body weights

The results of the analyses on body weights (IMW and W) are given in Table 2. The effects of inbreeding on the two measurements of body weight were opposite to each other. The decrease of IMW clearly demonstrates the inbreeding depression. According to Falconer and Roberts (1960), there is a possibility for late body weights to increase on inbreeding. The counterbalance of decline of number born (including the zero births) is one of the factors that decide the changes of body weight. This explains the increase of W as the level of inbreeding increased.

Response to selection

Having isolated the effect of inbreeding as described above, the true response to selection could be estimated. The selection response of LS was 0.05 pups born per generation. This is in agreement with the estimates given in literature (Hill, 1982; Vangen, 1993). Positive responses of 0.04 days decrease and 0.016 pups increase were observed for ILI and PPW traits respectively.

The genetic trend of LS (using average estimated breeding values) during 20 generation of selection is graphically presented in Figure 1. The response to selection over 20 generation was 0.98 pups. The range of estimated breeding values of the line was estimated to see the change of genetic variability during inbreeding. Reduction of genetic variability within each family could clearly be seen in all the families. Figure 2 illustrates this for one of the families.

An increasing pattern of correlated responses in IMW and W could be observed due to selection for high LS and low ILI.

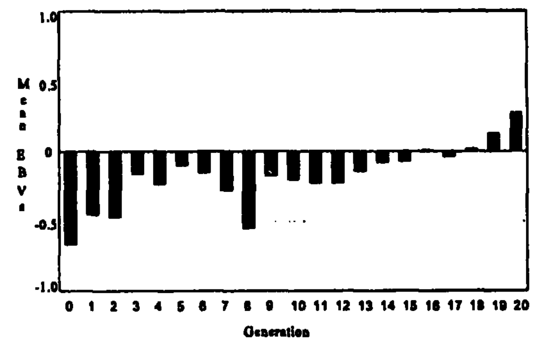

Figure 1. Genetic trend for litter size in IQS.

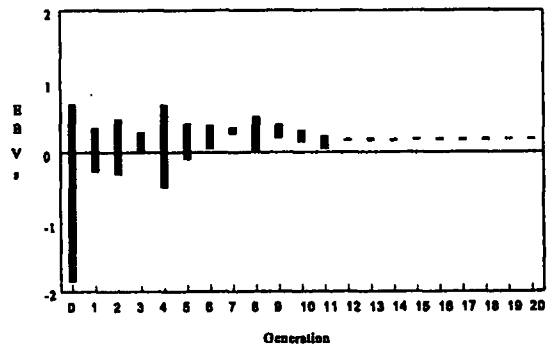

Figure 2. Changes of genetic variation (shown as range of EBV) in one of the families of IQS.

It was also interesting to note that the sum of the estimates of inbreeding depression and response to selection is in good agreement with phenotypic values observed. Therefore, the partitioning of the two opposing forces is consistent with the observed results.

As pointed out earlier, the present study simplifies the situation of inbreeding by introducing a linear effect of inbreeding depression in the animal model.

CONCLUSION

Since the result of inbreeding is opposed by the action of selection, direct regression of level of inbreeding on performance is a biased estimate of calculation of effect of inbreeding. Even though, the accounting for both additive and dominance effects in inbreeding analyses is more thorough option for such a situation, the present study followed only the incorporation of inbreeding coefficient of the animal as a fixed effect. This has enabled to disentangle two opposing forces and estimate the inbreeding depression and effects of selection. Therefore, it can be concluded that simple animal model with inbreeding coefficient as a fixed effect can also be used for simultaneous inbreeding and selection in the place of complicated estimations.

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