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Ovulation rate of lines of mice selected for testis weight

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SUMMARY

Selection was practised in two replicates for both high and low testis weight in the mouse. Typically 7 males were selected out of 30 recorded for a total of 5 generations. From an initial average of 191 mg the mean divergence between high and low lines reached 112 mg, with a realized heritability of 0·52. The ovulation rate of the lines changed in the same direction as that of selection, the mean divergence was 2·0 eggs in primiparous females in generation 4 and 1·6 in nulliparous females in generation 5. Correlated changes in the body weight of both sexes also occurred but were inadequate to account for the observed change in ovulation rate. The genetic regressions of ovulation rate on testis weight were estimated to be 2·9 and 1·4 eggs/100 mg in primiparous and nulliparous females, respectively, which, along with data from other experiments, correspond to genetic correlations between testis weight and ovulation rate of 0·50 and 0·25 respectively. There were no correlated changes in litter size. The possibility of using male testis size in breeding programmes to improve female reproductive performance is discussed.

1. INTRODUCTION

The same gonadotrophic hormones, follicle stimulating hormone (FSH) and luteinizing hormone (LH), are present in both male and female mammals, indicating that the genes controlling these hormones are expressed in both sexes (e.g. Cole, 1969). This conclusion is supported by the observation that single autosomal gene substitutions may change the somatic sex of an individual (Bishop, 1972). Evidence that the control of these genes is also partially common to both sexes has been obtained by measurement of the concentration of LH in the plasma of lambs of breeds or strains of sheep with differing levels of female performance (reviewed by Land, 1974). The gonad is the target organ for these hormones in both sexes, and in the male the response of the testis to hormonal stimulation is reflected in a change in size. It was therefore postulated that testis size in the male may be correlated with the ovarian activity of genetically related females (Land, 1973). The observations that testis growth is more rapid in male

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sheep of the Finnish Landrace breed, where the females have a high level of reproductive activity, than in those of the Tasmanian Merino breed where female reproductivity is low, and that the adult testis weight of lines of mice selected for ovulation rate was positively correlated with the ovulation rate of the lines, supported this hypothesis. Thus Land (1973) suggested that genetic improvements in female reproductive performance could be made by selection on traits such as testis size of the male.

The experiment with mice reported in this paper was designed to test this hypothesis by recording the ovulation rate of lines of mice while selecting for changes in testis size. There were two replicate populations, each with one line selected for high testis weight and one for low testis weight.

2. MATERIALS AND METHODS

(i) *Selection*

The lines were founded from unselected control lines A, B, E and F of generation 39 of the replicated selection experiment for body weight in the Q strain (Falconer, 1973). Thirty males and 30 females were taken at random from 10 to 14 full sib families of each line. Reciprocal pair matings were made between the representatives of lines A and B to form replicate 1 and between those of lines E and F to form replicate 2.

The progeny of the 4 males with the highest testis weight were selected from within the 30 males in each of the A × B and B × A crosses to form generation 1 of line 1 H, and those of the total of 8 males, 4 each from A × B and B × A with the lightest testes to form generation 1 of line 1 L. Similarly, lines 2 H and 2 L were formed by retrospective selection among the offspring of males in the E × F and F × E crosses (see Table 1).

In subsequent generations each selection line was maintained by mating *inter se*, female mates being picked at random except that full sib matings were avoided. Matings were made in pairs when the mice were 9 weeks of age. The families of approximately 1 in 4 males (Table 1) were selected for five generations using individual selection as practised in generation 0. No control lines were maintained.

(ii) *Traits*

Testis weight was scored *post mortem* at 11 weeks of age. The testes were dissected free of epididymis, blotted free of surface moisture and weighed on a Sartorius single pan balance. Results refer to the sum of weights of the two testes. The results of a preliminary study of the relationship between testis weight and body weight showed that the phenotypic correlation between testis weight and body weight varied from +0·55 to −0·44 among 5 of Falconer's (1973) control lines from generation 38, and from +0·61 to −0·11 between the males of the 4 lines of generation 39 which comprised the base population of the experiment (line A, 0·61; B, 0·29; E, 0·34; and F, −0·11). Pooled over lines and generations the correlation was 0·20 ± 0·06. Despite the overall positive phenotypic relationship

between the two, the variability between lines and the absence of estimates of the genetic relationship indicated that selection should be based on testis weight alone, and this was adopted.

Table 1. *Composition of the lines, the number of males whose progeny were selected as a fraction of the number recorded, and the number of females recorded each generation*

			Generation					
Replicate	Selection		0	1	2	3	4	5
1	High	Males	2 × (4/30)*	6/33	7/30	7/26	10/28	0/44
	1 H	Females	0	0	30	25	24	41
	Low	Males	2 × (4/30)*	7/31	6/28	6/27	10/29	0/37
	1 L	Females	0	0	26	25	28	40
2	High	Males	2 × (4/30)*	6/34	6/26	7/30	10/32	0/50
	2 H	Females	0	0	25	27	29	42
	Low	Males	2 × (4/30)*	6/30	7/26	7/27	11/30	0/43
	2 L	Females	0	0	25	27	28	41

* Four selected from 30 in both reciprocal crosses.

Litter size was recorded at birth as the number of young born alive in the first litter and at weaning at 3 weeks of age. The number per litter was not standardized. The ovulation rate, measured as described by Land & Falconer (1969), was recorded in generations 2, 3 and 4 in primiparous females at about 18 weeks of age, some 2 weeks after their litter was weaned, and in generation 5 in nulliparous females at about 9 weeks of age. The body weight of all males and females was recorded at 6 weeks of age, of males at approximately 11 weeks when they were scored for testis weight, and of females at 9 weeks when mated and at 18 weeks when scored for primiparous ovulation rate.

3. RESULTS

(i) *Testis weight*

The mean testis weight at generation 0 was 191 mg in both replicates (Table 2). The mean testis weight in each generation for each line is plotted in Fig. 1(*a*). The effects of high and low selection were apparently symmetric but in the absence of a control population this could not be verified The divergence in each generation between high and low lines is shown in Table 2 and plotted against the cumulative selection differential in Fig. 1(*b*). At generation 5 the high and low lines in the replicates differed by 114 and 110 mg in testis weight, about 60% of the base population mean. Since selection was practised in only one sex, estimates of the realized heritabilities were computed by doubling the estimates of the regression of cumulative response on cumulative selection differential, with the regression lines passing through the origin (Fig. 1*b*). Standard errors of realized heritabilities were calculated by adapting the method of Hill (1971, 1972), which allows for genetic drift, to selection on a single sex; this requires an estimate

of the variance of divergence in response to generation t which, assuming a constant population structure, is

$$2\sigma^2[th^2(1-h^2)/4M + th^4/4M^* + th^2/4F + (1-\tfrac{3}{2}h^4)/M^*],$$

where σ^2 is the phenotypic variance, h^2 the heritability, and M, F and M^* are the number of male parents, female parents and males scored per generation, respectively. Estimates of the realized heritability were $0{\cdot}54 \pm 0{\cdot}09$ and $0{\cdot}51 \pm 0{\cdot}09$ in replicates 1 and 2, respectively; the pooled estimate was $0{\cdot}52 \pm 0{\cdot}07$ (Table 3).

Table 2. *Means at generation 0 and differences between high (H) and low (L) lines in each replicate in subsequent generations for testis weight, female reproductive rate and body weight*

Generation	0	1	2	3	4	5
		Difference H – L				
	Mean					
Replicate 1						
Testis weight (mg)	191·5	23·4	45·9	89·1	83·2	114·0
Ovulation rate*	—	—	0·17	1·00	1·35	0·66
Litter size at						
Birth	9·76	0·42	−1·70	−0·50	−1·52	—
Weaning	8·34	1·22	−1·28	−0·96	−1·22	—
Body weight (g)						
♂ + ♀ 6 weeks	20·73	−0·78	−0·64	1·33	0·39	1·27
♀ 9 weeks	22·34	−0·01	0·00	0·91	−0·05	0·45
♂ 11 weeks	28·64	−0·33	−0·23	1·79	−0·69	1·83
♀ 18 weeks	—	—	−0·71	0·28	0·64	—
Replicate 2						
Testis weight (mg)	190·9	18·7	37·7	55·8	68·4	110·1
Ovulation rate*	—	—	2·04	2·85	2·64	2·47
Litter size at						
Birth	9·05	0·18	1·56	1·21	0·75	—
Weaning	7·47	0·78	1·39	1·51	0·98	—
Body weight (g)						
♂ + ♀ 6 weeks	20·29	0·74	2·35	0·75	1·80	2·33
♀ 9 weeks	21·34	−0·57	1·43	0·89	1·04	2·05
♂ 11 weeks	27·18	−0·90	0·08	1·81	2·71	3·08
♀ 18 weeks	—	—	2·38	1·96	2·39	—

* Generations 2, 3, 4, primiparous; 5, nulliparous.

(ii) *Ovulation rate*

The mean ovulation rates of primiparous females in generations 2, 3 and 4 and of nulliparous females in generation 5 are shown in Fig. 2(*a*) and the corresponding deviations between high and low lines are presented in Table 2. The ovulation rates of the lines selected for high testis weight exceeded those of the low selected lines by 1·35 and 2·64 eggs in primiparous ovulation rate at generation 4 in replicates 1 and 2, respectively, and by 0·66 and 2·47 eggs in nulliparous females at generation 5. The correlated response appeared to have occurred mainly in the high testis weight lines, but again this could not be verified in the absence of control lines.

The genetic regression of primiparous ovulation rate on testis size was calculated

from the regression of cumulative response in ovulation rate on cumulative response in testis weight using the deviation between high and low lines at generations 2, 3 and 4. The appropriate regression lines are illustrated in Fig. 2(*b*), and approximate standard errors of these estimates of the regression coefficients,

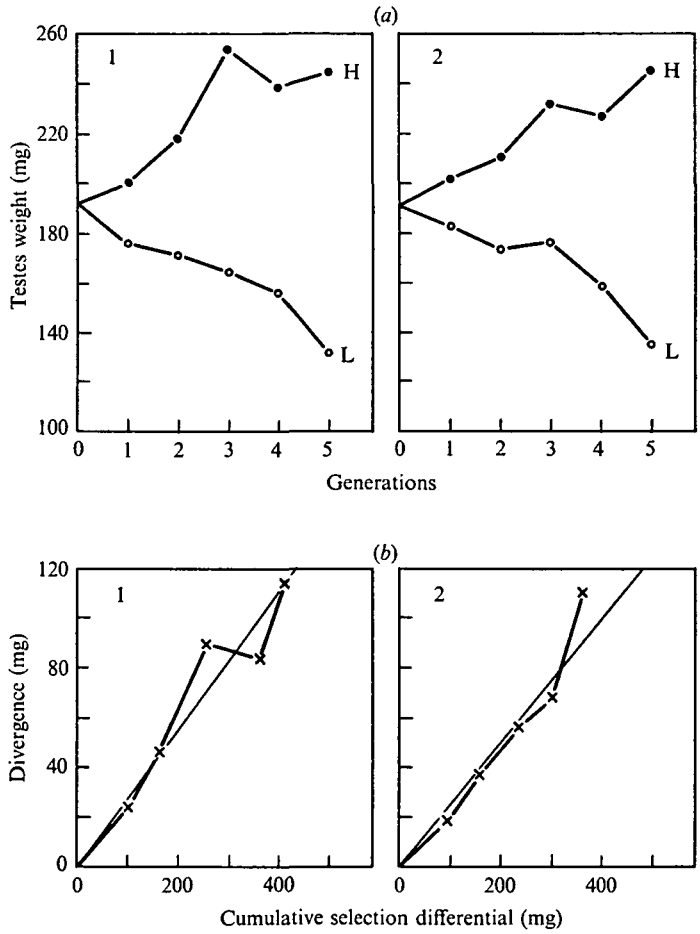

Fig. 1. The response of testis weight (*a*) to high (H) and low (L) selection in two replicates and (*b*) the divergence of both pairs of high and low lines plotted against the cumulative selection differentials, together with the linear regression of the responses on the selection differentials. 1, 2: replicates 1 and 2.

allowing for genetic drift, were computed from formulae of Hill (1971, 1972). The individual estimates (Table 3) were $1{\cdot}3 \pm 1{\cdot}0$ and $4{\cdot}5 \pm 1{\cdot}8$ giving a pooled value of $2{\cdot}9 \pm 1{\cdot}1$ eggs/100 mg. Although the estimates of the regression coefficients in the two replicates differed rather widely they were not significantly different ($P > 0{\cdot}05$). The genetic regressions of nulliparous ovulation rate on testis size were estimated by means of the ratio of their divergence between lines. The individual replicate estimates were $0{\cdot}6 \pm 0{\cdot}8$ and $2{\cdot}2 \pm 0{\cdot}8$ again rather different, but not significantly so, and gave a pooled value of $1{\cdot}4 \pm 0{\cdot}7$ eggs/100 mg (Table 3).

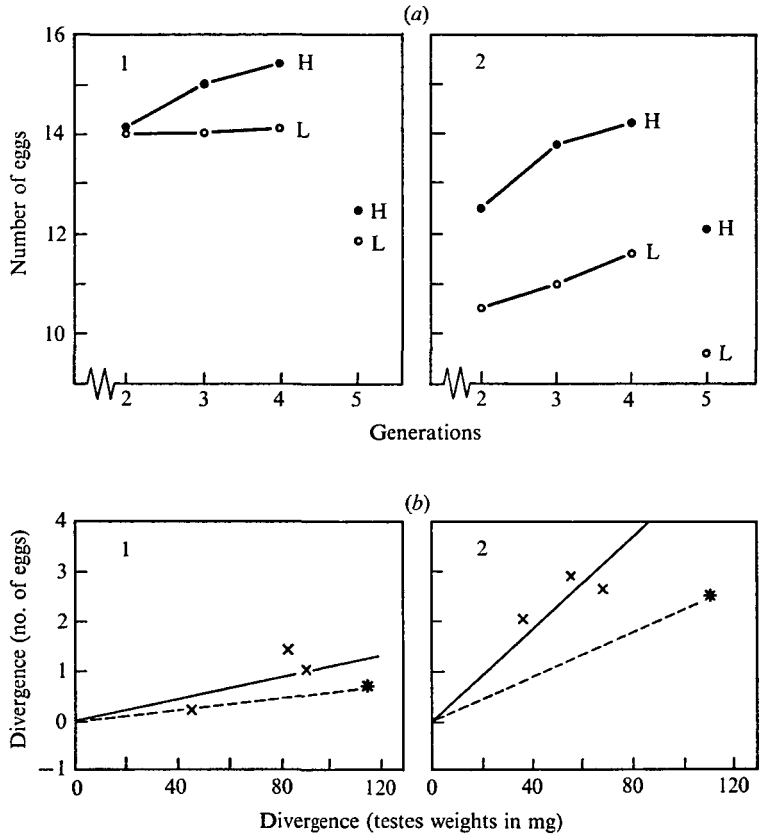

Fig. 2. (*a*) The ovulation rate of primiparous (generations 2, 3 and 4) and nulliparous (generation 5) females of the lines selected for high (H) and low (L) testis weight, (*b*) The divergence in ovulation rate (x primiparous, * nulliparous) between lines plotted against the divergence in tests weight, and the linear genetic regressions of ovulation rate (——, primiparous, – – –, nulliparous) on testis weight. 1, 2, replicates 1 and 2.

(iii) *Litter size and fertility*

Mean litter sizes at birth and at weaning of fertile matings are plotted in Fig. 3, and deviations between high and low lines are presented in Table 2. In replicate 2 litter size changed in the same direction as ovulation rate but to a smaller extent. In replicate 1, the line selected for high testis size had a lower litter size than the low selected line, although its ovulation rate was higher. In neither replicate, however, was the difference between lines statistically significant, nor was there a significant difference between replicates ($P > 0{\cdot}05$). This was reflected in estimates of the genetic regressions of litter size on testis weight which did not differ significantly from zero (Table 3).

There were few mating pairs which produced no young, 11 in the whole experiment; 7 of these occurred in 1 H, at least 1 in each of generations 1–4. Thus, if litter size is expressed per mating pair, the inferiority of 1 H, relative to 1 L is greater than in Fig. 3.

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Table 3. *Estimates of realized heritabilities and genetic regressions computed from the divergence between high and low selected lines, with approximate standard errors allowing for genetic drift*

	Estimates and standard errors		
	1	2	Pooled
Realized heritability of testis weight ...	0·54 ± 0·09	0·51 ± 0·09	0·52 ± 0·07
Genetic regression on testis weight of			
(*a*) Ovulation rate (eggs/100 mg)			
Primiparous	1·3 ± 1·0	4·5 ± 1·8	2·9 ± 1·1
Nulliparous	0·6 ± 0·8	2·2 ± 0·8	1·4 ± 0·7
(*b*) Litter size (young/100 mg)			
Birth	−1·4 ± 1·3	2·1 ± 1·5	−0·2 ± 1·1
Weaning	−1·2 ± 1·4	2·3 ± 1·7	0·0 ± 1·1
(*c*) Body weight (g/100 mg)			
6 weeks	0·8 ± 0·6	2·4 ± 1·9	1·6 ± 0·9
9 weeks	0·4 ± 0·3	1·8 ± 1·4	1·1 ± 0·6
11 weeks	1·0 ± 0·8	2·8 ± 2·2	1·9 ± 1·1

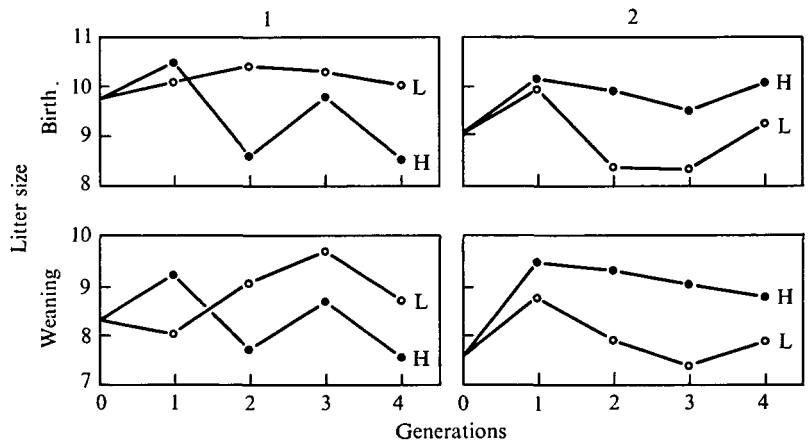

Fig. 3. The litter size (number of young) at birth and weaning of females of the lines selected for high (H) and low (L) testis weight. 1, 2, replicates 1 and 2.

(iv) *Body weight*

The mean body weight of each replicate in generation 0, and the corresponding deviations between high and low lines are presented in Table 2. Body weight tended to increase in both high and low lines in replicate 1 but not in replicate 2. The genetic regressions of body weight on testis weight were calculated as for litter size and are presented in Table 3. They are positive, at all ages in both replicates, and higher in replicate 2, but neither observation is statistically significant ($P > 0{\cdot}05$).

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4. DISCUSSION

The observed change in ovulation rate as a result of selection for testis weight demonstrates that a genetic change in female reproductive performance can be achieved by selection on male characteristics.

Testis weight changed by about 60% of the base value, or three phenotypic standard deviations, even though selection was only continued for five generations. The estimate of 0·5 for the heritability of testis weight is similar to that of 0·4 for testis growth in the sheep (Land, 1976) and suggests that a large proportion of the variation in testis size is additive genetic.

The change in ovulation rate of primiparous females was, relative to its mean, smaller than that of male testis size and, extrapolating the regression (Fig. 2*b*), would be predicted to be about three ova in generation 5, equivalent to 25% or 1·2 standard deviations; the change in nulliparous females was about half of that in primiparous females. The correlated change in body weight was only about 5% in one replicate and 10% in the other, equivalent to approximately 0·5 standard deviations on average.

Table 4. *Genetic parameters, estimated from Q strain mice*

	Testis wt (mg)	Body wt (g)	Primiparous ovulation rate
Genetic standard deviation	22[a]	1·7[b]	1·25[c]
Heritability	0·5[a]	0·36[b]	0·25[c]
Genetic repression on			
Testis wt (mg)	—	0·015[a]	0·03[a]
Body wt (g)	—	—	0·4[d]

Genetic correlation, body wt and testis wt: 0·20[a, b]

Source: a, This paper: b, Falconer (1973): c, Land and Falconer (1969); and d, Land (1970).

As a positive genetic correlation between body weight and ovulation rate has been reported (Bradford, 1969; Land & Falconer, 1969) the proportion of the change in ovulation rate which is independent of the change in body weight has to be established. The calculation of such a partial regression requires estimates of parameters unavailable from this experiment, and is therefore based on values obtained in previous studies on the Q strain of mice (Table 4).

The genetic partial regression of ovulation rate (O) on testis weight (T) holding body size constant, $b_{OT.W}$, was computed as $b_{OT.W} = (b_{OT} - b_{OW}b_{WT})/(1 - r^2_{WT})$, where b_{OT}, r_{WT}, etc., are the ordinary genetic regressions and correlations given in Table 4. The partial regression coefficient obtained for primiparous ovulation was 2·4 eggs/100 mg, compared with 2·9 eggs/100 mg for the ordinary regression. The corresponding figures for nulliparous ovulation rate were 1·0 and 1·4. Thus the greater part of the response in ovulation rate was independent of the change in body weight.

Again, combining information from the different selection experiments (Table 4),

the genetic correlation between testis weight and primiparous ovulation rate was estimated to be $0{\cdot}50 \pm 0{\cdot}18$ and between testis weight and nulliparous ovulation rate to be $0{\cdot}25 \pm 0{\cdot}20$, with standard errors based on the methods of Hill (1971). Whilst the standard error is approximate, the results suggest that there was a significant genetic correlation between testis weight and at least primiparous ovulation rate. The results therefore support the hypothesis that testis weight in the male is genetically correlated with ovulation rate in the female.

The observation of a correlated response in a trait sex-limited to females, together with the gradual, progressive change in testis weight, indicates that several autosomal genes were involved in the response in testis weight. It is therefore unlikely that a large proportion of the genetic variation in testis weight was controlled by the *Y* chromosome as reported for the difference between two inbred strains of mice (Haywood & Shire, 1975), but reciprocal crosses were not made between the high and low lines.

The responses in litter size were negligible, indicating that changes in embryonic mortality had accompanied the changes in ovulation rate. As in previous studies with the Q strain, the results suggest the presence of a positive genetic correlation between ovulation rate and embryonic mortality (Land, 1970). Changes in ovulation rate would not therefore be expected to lead to changes in litter size. Bradford (1972) suggesting that, in the mouse, natural ovulation provides the female with as many young as she can carry, so an increase in ovulation rate is of no benefit. In sheep and cattle, however, the situation is quite different; changes in the number of eggs present have a marked effect in litter size (Bradford, 1972; Ortavant & Thibault, 1970). If, therefore, testicular activity is correlated with ovarian activity in these species, the improvement of ovulation rate through selection on testis size would be expected to improve their litter size. The earlier observations of a correlation between testis growth and the ovulation rate of different breeds of sheep (Land, 1973; Land & Carr, 1975) indicate that the relationship between ovulation rate and testis size extends at least to sheep, and, with similar endocrine control of reproduction in other mammals, there is no reason to believe that it may not be a general relationship.

The changes in ovulation rate can be explained by Land's (1973) hypothesis that the quantitative control of the expression of genes controlling the release of gonadotrophic hormones is not sex limited. Direct tests for changes in hormone levels or tissue sensitivity were not attempted because of the technical difficulties with small mammals, and thus we can only infer that a common element of gonadal stimulation was changed in the present lines.

In animal-breeding programmes the improvement of reproductive traits is slow, partly because heritabilities are low, partly because traits are sex-limited, and partly because the reproductive rate itself is so low in species such as sheep, goats and cattle that a high proportion of females are needed to maintain the population. If, as the result of this experiment suggests, males can be selected on easily measured characteristics such as testis size that are correlated with ovulation rate, then more rapid response should be possible, particularly where most

selection pressure has to be practised among males. It is perhaps fortunate that it is simple to measure testis size, by callipers on the live animal, in species such as sheep and cattle where the advantages of selecting for testis size may be greatest, both in terms of increased selection intensity and the contribution of variation in ovulation rate to variation in litter size.

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