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Effects of selection on growth, body composition and food intake in mice

II. Correlated responses in reproduction

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SUMMARY

Female reproductive performance is reported in mice selected for ten generations for one of three criteria: either appetite (A), fat percentage (F) or total lean mass (P). For each criterion lines were selected for high (H) or low (L) performance, with contemporary unselected controls (C). In the A and P lines, litter size changed in the direction of the selected criterion, the changes being larger and more rapidly established in the A than in the P lines. At generation 10, the differences in litter size between high and low lines were 2·6 live young born in the A lines, and 1·0 live young born in the P lines. The differences in 6-week weight between the high and low lines were 3·5 g in the A lines, 6·5 g in the P lines. Changes in ovulation rate were the primary reason for changes in litter size, the differences between the high and low lines being 3·8 corpora lutea for the A lines, and 3·1 corpora lutea for the P lines. Fitting body weight at mating as a covariate within lines in the analysis of ovulation rate and live foetus number removed the differences between the high and low selected P lines, but not those in the A lines. The high and low selected A and P lines did not differ in prenatal survival. There were no consistent differences in litter size, ovulation rate or pre-natal survival in the F lines.

1. INTRODUCTION

Reproductive performance is important in determining profitability of many animal production systems, so its genetic determination and interrelationships with other major traits, namely growth rate, body composition and food intake are important to the animal breeder.

The mouse has been used extensively as a model to help understand the basic genetic and physiological mechanisms involved in traits of importance in larger mammalian species. Reproductive performance has been investigated in outbred populations of mice either by studying lines selected for litter size, or its components, ovulation rate and embryonic survival, or by studying it as a correlated trait to selection for other traits. In almost all published reports of reproductive performance as a correlated trait in mice, selection has been practised

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for body weight or growth rate (for reviews, see Roberts, 1965, 1979, and McCarthy, 1982). In these published studies, litter size has been used as a measure of reproductive performance, and has usually changed in the direction of selection (e.g. MacArthur, 1949; Falconer, 1953; Rahnefeld *et al.* 1966), but not in all cases (Bradford, 1971). Changes in ovulation rate in the same direction as changes in body weight have been shown to be the primary reason for the associated responses in litter size (MacArthur, 1944; Fowler & Edwards, 1960; Land, 1970), although the biological mechanisms involved in these relationships are not understood.

Lines of mice have been selected in our laboratory for one of three criteria, appetite, fat percentage or total lean mass (Sharp, Hill & Robertson, 1984). In this paper the correlated responses in litter size after ten generations of selection are reported. To understand these responses in litter size more fully the major components of litter size, namely ovulation rate and pre-natal survival were investigated.

2. MATERIALS AND METHODS

(i) *Selection lines*

Mice were selected for one of the three criteria: appetite (A) measured as 4- to 6-week food intake, corrected by phenotypic regression for 4-week body weight, fat percentage (F), using the ratio of gonadal fat pad weight (GFPW)) to body weight (BW) in 10-week-old males, and total lean mass (P), using the index BW $-$ (8 $\times$ GFPW) in 10-week old males.

For each selection criterion, there were three contemporary lines, one selected for high (H) performance, one for low (L) performance together with an unselected control (C). These lines were replicated three times (replicates 1, 2 and 3) for each of the three selection criteria. Thus, there were 27 lines maintained in all: 3 selection criteria $\times$ 3 replicates $\times$ 3 directions (H, L and C). Sixteen pair matings were made in each line up to generation 8; subsequently 8 pair matings were used. Selection was practised within litters. In the A lines, both sexes were selected. In the F and P lines, females were taken at random.

A full account of the origins of the mice, selection procedures and the responses obtained in growth, food intake and body composition for the first 11 generations, is given by Sharp *et al.* (1984). Each generation, 6-week weights, litter size at birth (number of live young) and those born dead were recorded in all the lines.

Mothers of generations 4 and 10 were given terramycin antibiotic in the water supply for the first week post-partum. This was done to alleviate the effects of an unidentified disease which caused ill-thrift in suckling litters and, in acute cases, death of the mother during the peak of lactation.

(ii) *Analysis of ovulation rate and pre-natal survival*

Mice and management. Random samples of mice not chosen as parents for the selection lines were taken from each of the 27 lines (replicates 2 and 3 from generation 9 and replicate 1 from generation 10) and pair mated to produce mice for measurement in this study. These mice were thus contemporaries of those used for breeding in generations 10 (replicates 2 and 3) and 11 (replicate 1) of the selection lines. In addition, a small number of mice not chosen for matings in generation

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10 and 11 of the selection lines were used; in the *A* lines these mice had been measured for the selection criterion. Mothers of generation 10 (Replicate 2 and 3), but not generation 11 (Replicate 1) were given Terramycin antibiotic in their water supply for the first week post-partum. As in the main selection lines, litters were adjusted to between 6 and 12 pups at birth, weaning took place at 21 days of age when the sexes were separated, and weaned mice were held in stock cages (no more than 6 mice in each cage) until mating time.

Females were weighed and mated at 8 weeks of age except in replicate 3 of the *F* lines which were weighed and mated at 7 weeks, by mistake. Two females were mated to each male, except where close inbreeding could be avoided by pair mating or mating three females to each male. Allocation of mates was similar to a scheme designed by Falconer (1973). The set of three lines, *H*, *L* and *C* of each replicate of each selection criterion were contemporaneous, as during the selection experiment.

Dissection technique. Vaginal plugs were used to indicate the day of conception, and females were dissected after 17 days to measure ovulation rate and pre-natal survival. Ovulation rate was estimated by counting the number of corpora lutea on each ovary under a dissection microscope.

This method is liable to underestimate ovulation rate, particularly when the corpora lutea are numerous, because of the difficulty of distinguishing between one large corpus luteum and two adjacent and partially confluent ones. To improve the accuracy of the count, each corpus luteum was dissected out under the binocular microscope with an eye surgeon's scalpel. In 17 out of the 556 pregnant mice studied (3·1 %) there were more implants in one horn of the uterus than corpora lutea counted on the adjacent ovary; in these cases the latter count was adjusted upwards to equal the number of implants. Although migration of embryos from one horn of the uterus to the other (McLaren & Michie, 1954) or polyovular follicles (e.g. Kent, 1960) might account for the discrepancy, we consider an error in counting to be a much more likely cause. As this is revealed only where there is no pre-implantation in one or both horns of the uterus, a count of corpora lutea could underestimate ovulation rate in more than the 3·1 % of cases corrected; but because all lines were counted in the same way, this bias should not seriously affect the conclusions (as argued by Falconer & Roberts, 1960).

The number of live foetuses and post-implantation losses (moles + resorptions + dead foetuses) were also recorded, and percentage survival computed as the ratio of live foetuses to corpora lutea.

Statistical analysis. Body weight, ovulation rate, live foetus number and pre-natal survival were subjected to analyses of variance by least squares. The main model fitted to the data was:

$$Y_{ijklm} = \mu + T_i + D_{ij} + R_{ik} + L_{ijk} + F_{ijkl} + e_{ijklm},$$

where Y_{ijklm} is the observation on the *m*th individual of the *l*th full-sib family of the *k*th replicate of the *j*th direction of selection and the *i*th selection criterion. Also: μ is the overall mean; T_i is the effect of the *i*th selection criterion ($i = 1, 2, 3$ corresponding to *A*, *F* and *P*); D_{ij} is the effect of the *j*th direction of selection ($j = 1, 2, 3$ corresponding to *H*, *L* and *C*) within the *i*th selection criterion; R_{ik}

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is the effect of the kth replicate ($i = 1, 2, 3$) within the ith selection criterion; L_{ijk} is the effect of the individual line and is used to estimate the effects of drift; F_{ijkl} is the full-sib family effect; and e_{ijklm} is the residual within full-sib family effect.

Directions of selection and replicates were tested against lines, pooled over selection criteria.

In further analyses, terms were also added for linear regression on body weight and/or ovulation rate of the individual mouse.

(iii) *Repeat sampling of Replicate 2 of the A lines*

The mice used in replicate 2 of the *A* lines were thought unrepresentative, as indicated by their body weights (see Results). Therefore, using the same procedures an additional study was conducted on this replicate on progeny of mice not selected for generation 12 in each selection line. The mothers of dissected mice did not receive Terramycin antibiotic.

Both the original and the repeat samples contributed to the results analysed, with the repeat sample included as an extra replicate. The bias created by this procedure was corrected for by reducing the sums of squares for the main effect of replication and the interaction of replication with direction of selection (called 'lines').

3. RESULTS

(i) *Correlated responses in litter size*

The mean litter sizes each generation from 0 to 10 are shown in Figs. 1–3, for each replicate and for the mean over replicates. To conform with the graphs of Sharp *et al.* (1984), litter size is plotted against the generation number of the *progeny*, and represents the reproductive performance of the *previous* generation of parents.

There was a rapid initial decrease in litter size in all lines. A decrease could be expected between generations −1 and 0 (0 and 1 of the progeny, Figs. 1–3), as those of generation −1 were a three-way cross (Sharp *et al.* 1984) with maximum heterosis for litter size. Subsequently, assuming unrelated founder animals, the range in inbreeding coefficients for lines at generation 10 was 5·7 %–9·0 %, with a mean of 6·8 % and no consistent difference in breeding between selection criteria, directions of selection or replicates. As Falconer's (1973) scheme for minimal inbreeding was used in the selection lines, no inbreeding accrued until generation 4, so inbreeding can not explain the initial decline in reproductive performance. A more likely source of the decline in litter size in the early generations of selection could have been a general decline in the health of the mice, as evidenced by very small young at weaning time and, in acute cases, by deaths of suckling females. Terramycin antibiotic was administered to the mothers of generation 4 and 10, and the offspring of generation 4 had, on average, larger litters than the previous generations.

Large and consistent differences in litter size between the high, low and control *A* lines were rapidly established. There were smaller but consistent differences between the high and low *P* lines, but no consistent differences among the *F* lines.

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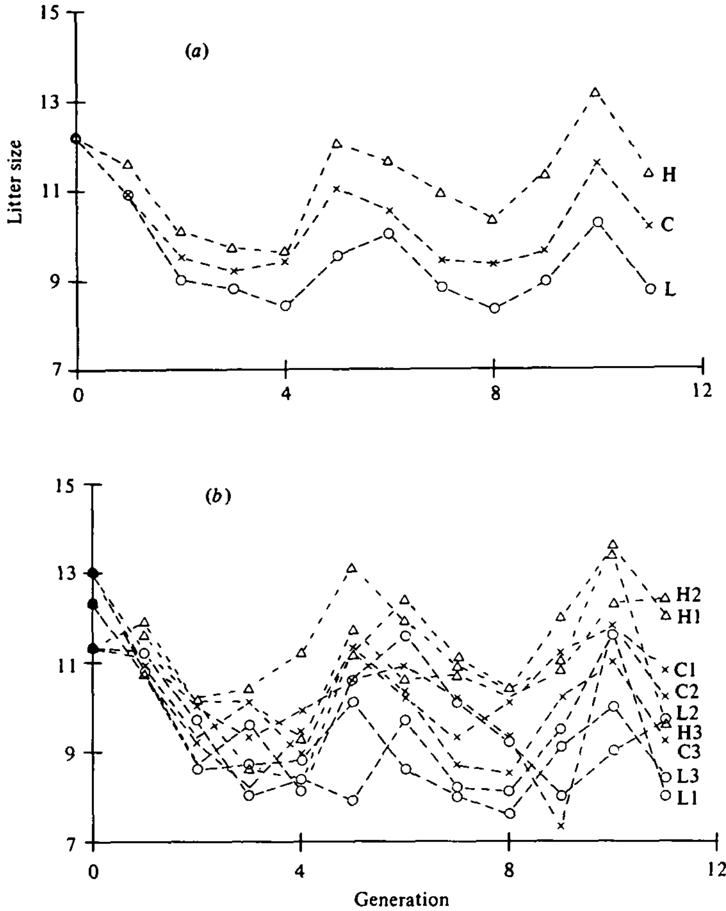

Fig. 1. *A* (appetite) lines: litter size for (*a*) mean of all replicates, (*b*) individual replicates. Generation numbers are those of the progeny to correspond with those of Sharp *et al.* (1984).

Table 1. *Mean of selected character and female 6-week weight in each set of lines at generation 10 (replicates pooled)*

Selection criterion	Direction of selection: High	Control	Low	High −Low
A (adjusted food intake) (g)*	66·3	63·3	57·5	+ 8·8
6 weeks wt (g)	26·0	23·4	22·5	+ 3·5
F (gonadal fat pad wt/body wt)† (mg/g)	20·5	14·0	8·7	+11·8
6 weeks wt (g)	23·6	23·7	22·2	+ 1·4
P (body wt − 8 × gonadal fat pad wt)† (g)	34·8	29·0	25·6	+ 9·2
6 weeks wt (g)	26·7	22·8	20·2	+ 6·5

* Adjusted food intake (g): FI + 1·65 (16·1 − w) for females, FI + 2·21 (17·8 − w) for males, where FI = 4–6 weeks food intake (g), w = 4 weeks wt (g).

† Body weight and gonadal fat pad weights measured in males at 10 weeks of age.

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The difference between the high and low *A* lines in litter size of generation 10 females is 2·6 young born, although the direct character under selection in the *A* lines has changed relatively less than the selected characters in the *P* and *F* lines (see Table 1). There is a consistent trend of changes in litter size relative to responses in the selected character appetite, in the *A* lines (Fig. 4). The corresponding graph for the *P* lines is shown in Fig. 5, but no plot has been given for the *F* lines where changes in reproductive rate were very small.

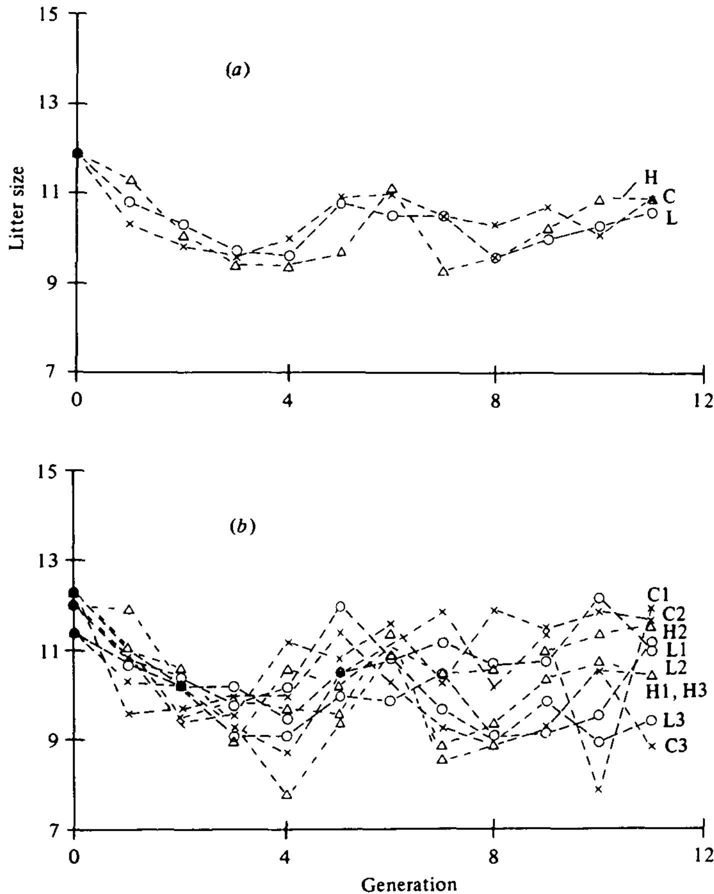

Fig. 2. *F* (fat) lines: litter size for (*a*) mean of all replicates, (*b*) individual replicates, as Fig. 1.

At generation 10, the mean difference in 6-week weight of females between high and low selected lines was 3·5 g for the *A* and 6·5 g for the *P* lines (Table 1). However, despite these larger differences in female body weights in the *P* compared to the *A* lines, the subsequent difference in litter size between the high and low *P* lines was only 1·0 young born.

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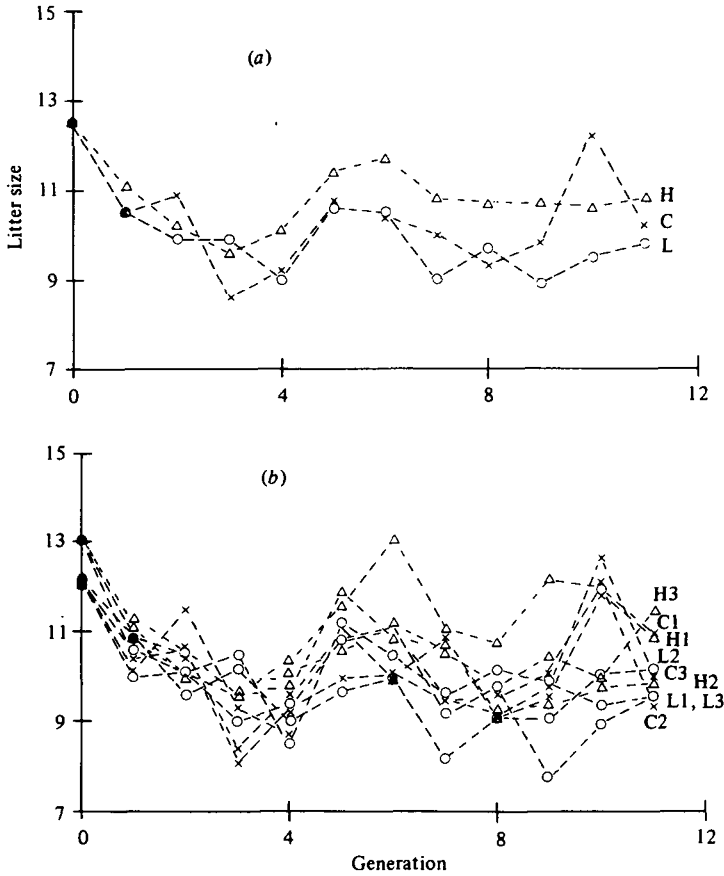

Fig. 3. *P* (protein) lines: litter size for (*a*) mean of all replicates, (*b*) individual replicates, as Fig. 1.

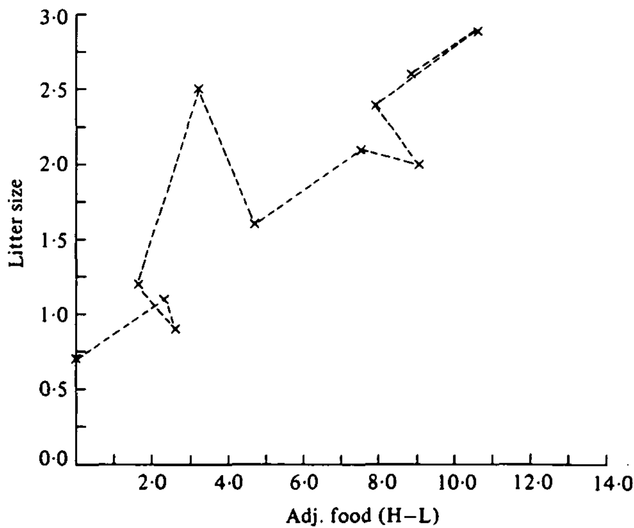

Fig. 4. *A* lines: high–low divergence of litter size plotted against high–low divergence of adjusted food intake (g) for the mean of all replicates.

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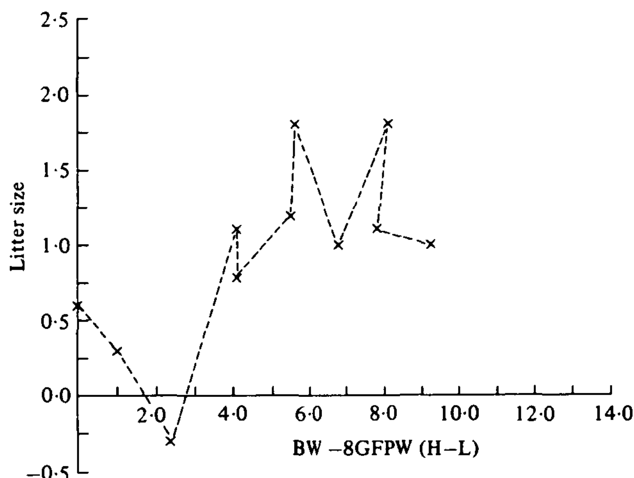

Fig. 5. P lines: High-low divergence of litter size plotted against high–low divergence of body weight $-8\times$ gonadal fat pad weight (g) for the mean of all replicates.

(ii) *Ovulation rate and pre-natal survival*

Results for ovulation rate and pre-natal survival are given for individual replicates in Table 2 and for replicates pooled in Table 3. The analyses of variance are summarized in Table 4 together with the linear constrasts to estimate divergence $(H-L)$ and symmetry $((H+L)/2-C)$ of response, which were almost orthogonal.

The body weight of females at mating, their ovulation rate and live foetus number were significantly higher in the high than in the low A lines, and although pre-natal survival decreased slightly in the high lines, the difference from the low lines was not significant. A similar situation was observed for the P lines, except that relative to the A lines, the differences between the high and low lines were larger for body weight at mating and smaller for ovulation rate and live foetus number. The responses in litter size can therefore be explained by changes in ovulation rate rather than pre-natal survival.

Although the body weight of females at mating was significantly heavier in the high than in the low F lines, ovulation rate and live foetus number were not different. Pre-natal surival was slightly higher in the high lines, but the difference from the low lines was not significant.

The linear regression of ovulation rate and live foetus number on body weight at mating (which is a phenotypic, within line regression) completely removed the differences between the high and low P lines, but removed only some of the differences between the high and low A lines.

For the F lines, where the high lines were heavier than the lows, fitting body weight at mating as a covariate the high (fat) lines appeared to have a lower reproductive rate than the lows.

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Table 2. *Means for body weight at mating (g) (B.W.), ovulation rate (O.R.), live foetus number (L.F.) and pre-natal survival % (P.S.) (numbers of mice for each mean varied from 14 to 24)*

	Replicate 1				Replicate 2				Replicate 3			
Lines	B.W.	O.R.	L.F.	P.S.	B.W.	O.R.	L.F.	P.S.	B.W.	O.R.	L.F.	P.S.
A (adjusted food intake)												
High	28·3	16·9	12·8	80·3	24·6	12·8	11·2	86·8	30·4	17·1	13·4	79·2
Control	24·1	11·9	8·8	73·4	26·1	13·3	11·1	84·0	25·2	11·2	9·4	82·1
Low	24·5	11·9	10·2	86·6	26·8	13·7	11·6	85·4	25·0	12·2	10·1	83·2
A (adjusted food intake)												
High*	—	—	—	—	30·8	15·8	11·5	73·5	—	—	—	—
Control*	—	—	—	—	24·2	11·9	9·7	81·8	—	—	—	—
Low*	—	—	—	—	24·7	9·6	7·5	78·8	—	—	—	—
F (gonadal fat pad wt/body wt)												
High	27·3	12·4	9·6	78·0	27·9	16·2	13·3	83·1	23·4	11·6	10·0	87·5
Control	26·0	13·2	10·0	76·7	27·6	15·5	12·3	79·4	24·2	11·9	10·0	84·8
Low	23·1	14·3	10·3	75·1	24·2	14·2	11·4	80·0	22·1	11·7	9·4	81·9
P (body wt $-8\times$ gonadal fat pad wt)												
High	29·2	14·8	11·6	78·1	28·3	13·4	11·0	82·5	30·4	15·7	12·6	80·8
Control	20·7	10·8	8·9	82·8	25·0	12·6	10·2	80·8	24·9	12·8	9·9	78·1
Low	21·3	11·3	9·5	84·8	22·3	12·1	10·6	87·5	21·5	11·2	9·2	82·9

* Repeat study.

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Table 3. *Numbers of mice mated and means of body weight (g) (B.W.), ovulation rate (O.R.), live foetus number (L.F.) and pre-natal survival % (P.S.) (replicates pooled)*

Lines	No. of mice mated	No. of pregnant mice	No. of non-pregnant mice*	Means B.W. (g)	O.R.	L.F.	P.S. (%)
			A (adjusted food intake)				
High	71	70	1	28·5	15·6	12·2	79·9
Control	74	73	1	24·9	12·0	9·7	80·3
Low	77	77	0	25·2	11·8	9·8	83·5
			F (gonadal fat pad wt/body wt)				
High	62	61	1	26·2	13·4	11·0	82·9
Control	55	51	4	25·9	13·5	10·8	80·3
Low	54	54	0	23·1	13·4	10·4	79·0
			P (body wt − 8 × gonadal fat pad wt)				
High	63	62	1	29·3	14·6	11·7	80·5
Control	59	54	5	23·5	12·1	9·7	80·6
Low	55	54	1	21·7	11·5	9·8	85·1
S.E.†				0·70	0·72	0·53	2·93

* Non-pregnant mice are not included in the analyses.

† Standard errors based on between-line variance (except for pre-natal survival, where it was based on the combined variance of between-lines and between-full-sib family effect).

Repeat sampling of replicate 2 of the A lines

Some circumstantial evidence that the original sampling was unrepresentative comes from comparisons between body weights at mating of 8-week old females in the sample originally dissected, 24·6, 26·1 and 26·8 g for *H*, *C* and *L*, respectively, and body weights of 6-week old females in the selection experiment, 25·7, 22·2 and 24·8 g respectively. Likewise, live foetus numbers in the samples were 11·2, 11·1 and 11·6 respectively and 12·4, 11·1 and 9·7 live young in the selection lines. The high *A* line in replicate 2 is the only one out of the 27 lines where the 8-week weights of the sample were lower than the 6-week weights from the selection experiment. Assuming a phenotypic regression of at least +0·4 eggs per gram increase in body weight at mating (Land, 1970; table 4), it is not surprising that ovulation rate and live foetus numbers were slightly lower in the original sample of the high than the control or low line samples of replicate 2.

The results in the repeat sampling of this replicate were quite different from those obtained previously in both body weight and reproductive performance (Table 2), and were more comparable to the results of the selection experiment (Fig. 1, table 1).

4. DISCUSSION

Our results show that changes in ovulation rate, rather than pre-natal survival, are responsible for the changes in litter size in the lines selected for appetite and total lean mass. In contrast, mice selected for percentage fat do not display significant changes in litter size or ovulation rate.

The index used as the selection criterion in the total lean mass lines (body

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Table 4. *Linear contrasts for differences between high and low selected lines (H–L) and symmetry, ((H+L)/2-C) and analyses of variance for body weight (g) (B.W.), ovulation rate (O.R.), live foetus number (L.F.) and pre-natal survival (%) (P.S.), before and after fitting regressions on body weight or ovulation rate*

		No. regressions fitted				Regressions fitted		
						B.W. Fitted		O.R. Fitted
Contrast	d.f.	B.W. (g)	O.R.	L.F.	P.S. (%)	O.R.	L.F.	P.S. (%)
		Contrasts				Contrasts		
A H–L	1	+3·3**	+3·8**	+2·4**	−3·6	+2·1**	+1·6*	+2·2
A Symmetry	1	+1·4*	+1·1*	+0·9**	+1·0	+0·4	+0·5	+2·7
F H–L	1	+3·1**	0·0	+0·6	+3·9	−1·6	−0·2	+3·9
F Symmetry	1	−1·3	−0·2	−0·1	+0·7	+0·5	+0·2	+0·4
P H–L	1	+7·6**	+3·1**	+2·0*	−4·6	−0·8	+0·1	+0·1
P Symmetry	1	+2·0*	+1·0	+1·1	+2·2	0·0	+0·6	+3·8
						Regression coefficients (±S.E.)		
Covariate								
B.W.	1	—	—	—	—	0·49**±0·061	+0·41**±0·072	—
O.R.	1	—	—	—	—	—	—	−1·3**±0·37
		Mean squares				Mean squares		
Replicates	6	77·77*	67·72*	39·99	357	23·54	23·00	300
Lines	12	24·11	22·54*	13·73	143	14·46**	10·57	201
Families	144	13·28**	9·85**	9·62**	447**	6·23**	9·71**	416**
Individuals								
No regressions	382	3·11	5·13	6·62	284	—	—	—
Regressions fitted	381	—	—	—	—	4·38	6·11	276

*$P < 0·05$, **$P < 0·01$, otherwise $P > 0·05$.

Tests: Contrasts, main effects and (pooled) replicates against (pooled) lines, (pooled) lines against families and families against individuals.

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weight–8 × gonadal fat pad weight) has a very high correlation with body weight and the correlated changes in litter size agree in magnitude with those reported in selection studies on body weight or body weight gain (MacArthur, 1949; Falconer, 1953; Fowler & Edwards, 1960; Rahnefeld *et al.* 1966; McCarthy, 1982), as do the changes in ovulation rate (MacArthur, 1944; Fowler & Edwards, 1960; Land, 1970).

However, the correlated changes in ovulation rates from selection for appetite are larger than can be explained simply as a consequence of increases in body weight: For every gram increase in body weight at mating there is an increase of 1·15 corpora lutea in the *A* lines but an increase of only 0·41 in the *P* lines. The significant asymmetry in body weight, ovulation rate and live foetus number of the *A* lines could be real, but may have been partly due to the relatively low performance of the control mice within the sample dissected, compared to control mice used in other generations.

Fowler & Edwards (1960) have suggested from indirect evidence that ovulation rate in the mouse may be correlated more with body protein weight rather than total body weight. Sharp *et al.* (1984) found that mice from the high *A* line have become leaner than control mice, but these relatively small differences in carcass composition would only be enough to explain a small part of the higher ovulation rates observed. Further, the *F* lines with substantially changed composition and significant changes in body weight have shown little change in reproductive performance. So, what could be causing the high correlated responses in reproduction within the *A* lines? The following explanations are offered as possibilities:

(1) A major gene or genes with large effects on ovulation rate could have been present in the base population, as suggested by the early rapid response in litter size (Figs. 1 and 4). The evidence for this is, however, unconvincing. The variance of litter size within lines did not show a decline after the first few generations as would be expected following fixation of a major gene. In the study of ovulation rate and pre-natal survival, however, a large variance relative to other lines was noticed for ovulation rate in replicate 1 of the high *A* line, but this was not consistent for litter size over many generations.

(2) The high *A* line mice may ovulate more eggs in response to the dynamic effect of consuming relatively large amounts of food ('flushing').

(3) Mice are measured for food intake from 4 to 6 weeks of age. This period encompasses the onset and attainment of puberty, a process which may be physiologically associated with the determination of ovulation rate, general metabolism and of appetite. It is possible that selection for high appetite produced mice which reach their 'peak' of reproductive potential earlier in life than lines selected for body weight, or components thereof.

(4) There may be some pleiotropy between genes controlling food intake and metabolic rate and those controlling ovulation rate. We have evidence of differences in metabolic rate between the high and low appetite selections (S. Bishop, unpublished; M. Nielsen, unpublished).

Interestingly, the increases in ovulation rate in the high A lines is reflected in larger litter sizes, and has not led to a significant decline in pre-natal survival. A decline in pre-natal survival with increasing ovulation rate has been noted in previous studies (e.g. Bowman & Roberts, 1958; Fowler & Edwards, 1960). Our

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results can be contrasted with the effects of direct selection where, although ovulation rate has been increased, litter size remained unchanged (Land & Falconer, 1969; Bradford, 1969).

In conclusion, directional selection for appetite and total lean mass in mice has resulted in changes in litter size and ovulation rate in the same direction as selection, those selected for appetite showing the larger responses. Associated changes in body weight can explain the differences in ovulation rate and litter size in the lean mass lines, but can only partly explain the differences in the appetite lines. Lines selected for percentage fat showed no correlated response in litter size or ovulation rate. The reasons for the large responses in ovulation rate within the appetite lines obviously need closer study.

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REFERENCES

Bowman, J. C. & Roberts, R. C. (1958). Embryonic mortality in relation to ovulation rate in the house mouse. *Journal of Experimental Biology* **35**, 138–143.

Bradford, G. E. (1969). Genetic control of ovulation rate and embryo survival in mice. I. Response to selection. *Genetics* **61**, 905–921.

Bradford, G. E. (1971). Growth and reproduction in mice selected for rapid body weight gain. *Genetics* **69**, 499–512.

Falconer, D. S. (1953). Selection for large and small size in mice. *Journal of Genetics* **51**, 470–501.

Falconer, D. S. (1973). Replicated selection for body weight in mice. *Genetical Research* **22**, 291–321.

Falconer, D. S. & Roberts, R. C. (1960). Effect of inbreeding on ovulation rate and foetal mortality in mice. *Genetical Research* **1**, 422–430.

Fowler, R. E. & Edwards, R. G. (1960). The fertility of mice selected for large or small body size. *Genetical Research* **1**, 393–407.

Kent, H. A. (1960). Polyovular follicles and multinucleate ova in the ovaries of young mice. *Anatomical Record* **137**, 521–524.

Land, R. B. (1970). Genetic and phenotypic relationships between ovulation rate and body weight in the mouse. *Genetical Research* **15**, 171–182.

Land, R. B. & Falconer, D. S. (1969). Genetic studies of ovulation rate in the mouse. *Genetical Research* **13**, 25–46.

MacArthur, J. W. (1944). Genetics of body size and related characters. II. Satellite characters associated with body size in mice. *American Naturalist* **78**, 224–237.

MacArthur, J. W. (1949). Selection for small and large body size in the house mouse. *Genetics* **34**, 194–209.

McLaren, A. & Michie, D. (1954). Transmigration of unborn mice. *Nature* **174**, 844.

McCarthy, J. C. (1982). The laboratory mouse as a model for animal breeding: a review of selection for increased body weight and litter size. *Proceedings of the 2nd World Congress on Genetics Applied to Livestock Production, Madrid* **5**, 66–83.

Rahnefeld, G. W., Comstock, R. E., Singh, M. & Na Puket, S. R. (1966). Genetic correlation between growth rate and litter size in mice. *Genetics* **54**, 1423–1429.

Roberts, R. C. (1965). Some contributions of the laboratory mouse to animal breeding research. Parts I and II. *Animal Breeding Abstracts* **33**, 339–353, 515–526.

Roberts, R. C. (1979). Side effects of selection for growth in laboratory animals. *Livestock Production Science* **6**, 93–104.

Sharp, G. L., Hill, W. G. & Robertston, A. (1984). Effects of selection on growth, body composition and food intake in mice. I. Responses in selected traits. *Genetical Research* **43**, 75–92.

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