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Effects of selection on growth, body composition and food intake in mice I. Responses in selected traits

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SUMMARY

Mice were selected for one of three criteria: appetite (A), measured as 4- to 6-week food intake, adjusted by phenotypic regression to minimize change in 4-week body weight, fat percentage (F), using the ratio of gonadal fat pad weight to body weight in 10-week-old males, and total lean mass (protein, P), using the index, body weight in 10-week-old males $-(8 \times$ gonadal fat pad weight). For each selection criterion, there were 3 high, 3 low and 3 unselected control lines. At generation 11, the high and low A lines diverged by 17% of the control mean and the realized heritability from within family selection of adjusted food intake was 15%. Selection for this character produced changes in body weight, gross efficiency from 4 to 6 weeks, and percentage of fat, the high lines being heavier, more efficient and less fat than the lows. The high and low F lines diverged by 80% of the control mean and the realized heritability of the ratio of gonadal fat pad weight to body weight was 44%. Selection for this character produced changes in total fat per cent, but little change in percentage protein, body weight, food intake or gross efficiency. The high and low P lines diverged by 40% of the control mean and realized heritability of the lean mass index (10-week weight $-[8 \times$ gonadal fat pad weight]) was 51%. Selection for an increase in the index increased body weight at all ages, food intake and 4- to 6-week gross efficiency. There was no change in percentage fat. Responses in the selected traits were not highly correlated, and the different lines provide an opportunity for investigating responses in physiology, metabolism and gene products.

1. INTRODUCTION

Growth rate, body composition and food intake are major input and output components in meat animal production enterprises, so their genetic determination and inter-relationships are important to the animal breeder. The extent of genetic variability in these traits in man is also relevant to the study of human obesity. Ideally we might undertake all the relevant genetic analyses in each of the species concerned, but cost or impracticalities rule this out. The mouse, with its low unit cost and short generation interval, enables a wide range of experimentation to be conducted which should be relevant to other mammalian species, provided the

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results are interpreted at the level of the basic physiology or genetic mechanisms and the study in mice is not regarded as an end in itself.

There have already been rather extensive selection experiments on growth rate and body weight in mice, rather less for appetite, little for composition and none for all three together. For reviews see Eisen (1974), Roberts (1979) and McCarthy (1982).

The first objective of this study was to produce, from the same base population, strains of mice which would be physiologically distinct in either growth rate or food intake or fatness. In practice, however, it was necessary to use a simple and quickly determined predictor of fatness, the weight of the gonadal fat pad in relation to body weight of 10-week-old males.

The unit of selection was three contemporary lines, the first selected upwards, the second downwards and the third an unselected control, each with the same breeding structure. Three replicates were maintained for each of the three selection objectives:

(i) the 'appetite' (A) lines, in which the high and low lines would differ in voluntary food intake in the growing period, but not differ in initial weight;

(ii) the 'fat' (F) lines, which would differ in proportion of body fat but not in body weight;

(iii) the 'protein' (P) lines, which would differ in lean mass but not in body weight.

Thus there were 27 lines maintained in all: 3 selection criteria × 3 replicates × 3 lines (high, low and control).

In this paper the results are reported for the traits actually under selection, which are therefore direct responses in one set of lines and correlated responses in the others, together with related traits such as body weights at different ages and body composition by chemical analysis. In subsequent papers the responses will be reported more deeply, for example at the level of ovulation rate, metabolic rate and hormonal levels.

The studies of correlated traits will utilize the power of the selection approach, in that large genetic differences can be produced so as to enable efficient analysis of traits which are expensive to measure. Provided selection lines are replicated, in order to distinguish between genetic drift (sampling) and selection effects, the source of the differences among the lines is known. In contrast, inbred lines also yield large genetic differences, but they result from some unknown combination of natural selection, artificial selection and drift.

2. MATERIALS AND METHODS

(i) *Mouse stock and management*

A new strain – the 'G' strain – was established for this experiment. Two inbred lines, JU and CBA, were crossed, and the F1 crossed to an outbred strain, CFLP, which was obtained from Carnworth laboratory in 1976. One generation of random mating followed the second cross, the next being designated generation 0 of the selection experiment.

From within the 16 full-sib families established for each of the three replicates

of each of the three selection treatments at generation 0, high (H), low (L) and control (C) mice were taken to start the lines. Subsequently each line consisted of 16 pair-matings per generation until generation 8, when they were reduced to 8 pair-matings. All selection was practised within litters using a mating scheme similar to that of Falconer (1973). To spread the technical work, matings were set up over an 11-week period in each generation, with a 4-week gap, approximately, between replicates, with the H, L, C set of any selection criterion × replicate combination kept as contemporaries. Litters were adjusted to between 6 and 12 young at birth, and weaned at 21 days. Mothers of generations 4 and 10 were given terramycin antibiotic in their water supply for the first week post-partum.

In generation 0 and for part of generation 1, the mice were fed on McGregor's Rat and Mouse Diet. The diet was changed to B.P.'s Rat and Mouse No. 1 Expanded Maintenance Diet (14·8% crude protein, 13·1 kJ/g metabolizable energy) between generations 1 and 2.

(ii) *Selection procedures*

'*Appetite*' or '*A*' lines

In the lines selected for food intake, selection was for individual 4 to 6-week food intake, adjusted for 4-week weight by the within-family, within-sex phenotypic regression of food intake on 4-week weight. The regression coefficients were recalculated in generation 2 after the diet change, and were 1·65 and 2·21 g food/g body weight for females and males, respectively. The mean 4-week weights were 16·1 and 17·8 g, respectively, at the start of the experiment, so food intake was adjusted to these weights by the following equations, which were used both during the selection and in assessing the responses (weights in g):

$$\text{females: adjusted food intake} = \text{food intake} + 1{\cdot}65\ (16{\cdot}1 - \text{4-week wt})$$

$$\text{males: adjusted food intake} = \text{food intake} + 2{\cdot}21\ (17{\cdot}8 - \text{4-week wt}).$$

In the high and low lines, individual food intake was recorded on four males and four females from each litter, and one mouse of each sex per litter was selected. In the control lines, only two mice of each sex per litter were recorded.

'*Fat*' or '*F*' lines

In the F lines the ratio of gonadal fat pad weight to body weight in 10-week-old males was used as the selection criterion. Gonadal fat pads are discrete depots, can be dissected out quickly and accurately, and the correlation between percentage gonadal fat pad weight and percentage total fat is high ($r = 0{\cdot}9$; Jagot *et al.* 1980; Rogers & Webb, 1980). Four males from each litter in the selected lines were killed, weighed and dissected at 10 weeks, having been mated about two weeks before. The offspring of the selected males were kept for the next generation. In the control lines, two males per litter were dissected at 10 weeks, one of them having been mated and its offspring kept for the next generation.

'Protein mass' or 'P' lines

In the lines selected for total lean mass, the selection criterion was the index (body weight (g) $-[8 \times$ gonadal fat pad weight (g)]). As the gonadal fat pads represent about one-eighth of the total fat in 10-week-old males, this index was used as a simple phenotypic predictor of fat-free mass, although it is very highly correlated ($r = 0{\cdot}94$) with 10-week weight. The selection procedure was identical to that used in the F lines.

(iii) *Measurement of correlated responses*

Body composition

In generation 7, two batches of eight mice, each comprising one randomly sampled 10-week-old male from each of eight litters from each line, were killed, the gut contents removed and freeze-dried. Chemical analyses of the batches were performed by the staff of the Rowett Research Institute. Dry matter and ash content were determined by heating freeze-dried samples to 100 °C, then 800 °C. Fat content was estimated by the chloroform–methanol technique (Atkinson *et al.* 1972), and protein content by difference.

Food intake

In generations 8 and 9, food intake from 4 to 6 weeks was recorded in the F and P lines, on approximately 30 mice of each sex per generation in each high and low line, and 15 in the control lines. At the same time, body weight and gonadal fat pad weight were recorded in 10-week-old males from the A lines, on approximately 15 males per generation in each high and low line, and 8 in the control lines.

(iv) *Data analysis*

Selection differentials were calculated as the average difference of each selected mouse from its litter–sex mean, weighted by the number of its progeny measured for the selected character in the next generation. As selection was carried out in only one sex in the P and F lines, the selection differentials calculated in these lines were halved. Realized heritabilities were calculated for generations 0–11 from the regression of response on cumulated selection differential. Selection differentials in the control lines were calculated, but were assumed to be zero for estimation of realized heritabilities.

Analyses of variance of body composition and food intake in generations when these traits were recorded in all lines were carried out using the model:

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

where Y_{ijkl} is the lth observation on the kth replicate of the jth direction of selection of the ith selection criterion. Also

μ is the overall mean;

T_i is the effect of the ith selection criterion ($i = 1, 2, 3$ corresponding to A, F and P);

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D_{ij} is the effect of the jth direction of selection ($j = 1, 2, 3$, corresponding to H, L and C) within the ith selection criterion;

R_{ik} is the effect of the effect of the kth replicate ($k = 1, 2, 3$) within the ith selection criterion;

L_{ijk} is the effect of the jkth line in the ith selection criterion; and

e_{ijkl} is random error, corresponding to batches ($l = 1, 2$) in the body composition trial or litters in other trials.

The variance due to lines (or direction × replicate within selection criteria interaction, L_{ijk}) was assumed to be due to random drift and was used for computation of standard errors and significance tests of responses. It was computed by pooling analyses over all selection criteria, assuming no heterogeneity of variance associated with selection criterion or direction. In the analyses the error variance, var (e_{ijkl}) was not necessarily estimated, because it was not used for the main tests. Contrasts, of divergence of response, H–L, and of asymmetry of response, $(H + L)/2 - C$, were tested within each selection criterion.

3. RESULTS

(i) *Direct responses to selection and realized heritabilities*

A lines

The results of eleven generations of selection for 4- to 6-week food intake, adjusted for 4-week weight, are shown in Fig. 1 both for the mean of the three replicates and for the three replicates separately, with values expressed as the adjusted food intakes averaged over males and females. As will be shown later, most of this response was due to change in food intake rather than 4-week weight.

The large drop in adjusted food intake between generations 0 and 2 was due to the change of diet, the new diet being more energetically dense than the old. The changes as a result of selection in the upward and downward direction were very similar. At generation 11 the high lines had increased by about 8·0 %, and the low lines had decreased by about 8·6 % of the controls, the total divergence being about 16·6 % or 1·9 phenotypic standard deviations. The replicates differed: the high–low differences at generation 11, as a percentage of the control mean, were 24·7 %, 10·6 % and 14·1 % for the three replicates.

Table 1 shows the total cumulated selection differentials in the lines. Responses, pooled over replicates, are plotted against cumulated selection differentials in Fig. 2. The realized heritabilities were calculated separately for each replicate from the regression of response on cumulated selection differential up to generation 11, with the responses taken as the deviation of the mean of the line from that of its control in the same replicate. The regression coefficients and their standard errors are given in Table 2. These standard errors were calculated assuming the standard regression model of independent errors with equal variances which, because the responses depend on cumulating drift effects, are biased (Hill, 1972). The sampling variance of the realized heritability averaged over lines was therefore also estimated empirically from the observed variance of the regression coefficient between the replicates, albeit with only two degrees of freedom. In Table 2 the

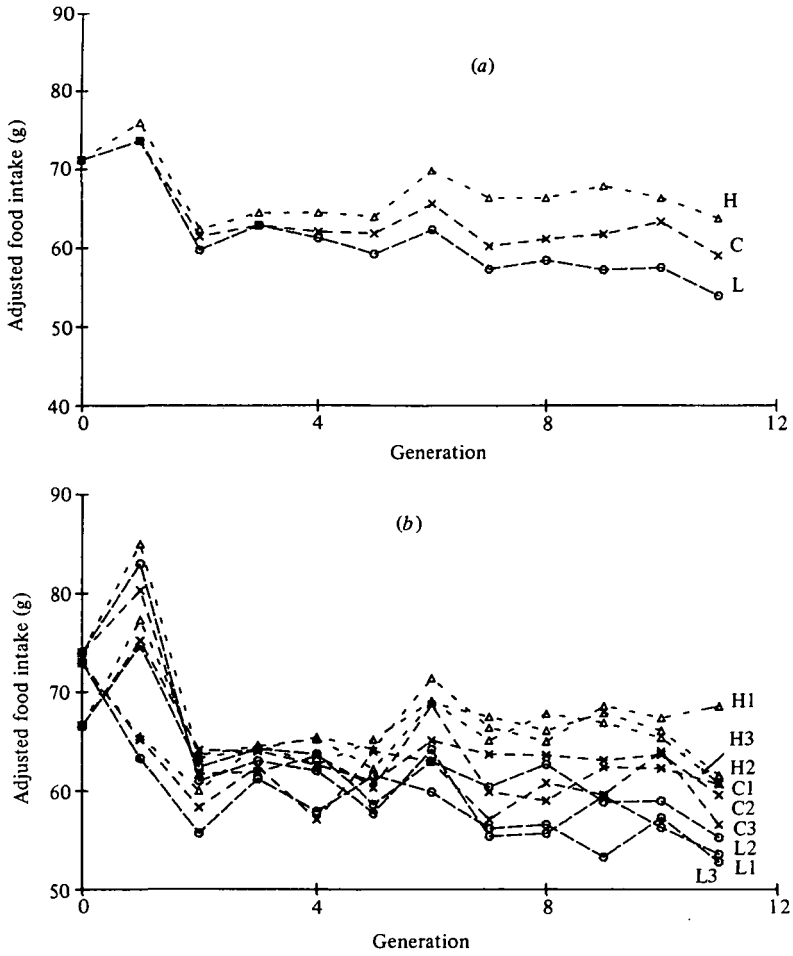

Fig. 1. A (appetite) lines: adjusted food intake for (*a*) mean of all replicates, (*b*) individual replicates.

'pooled' estimates are the regression of the mean of lines on the mean selection differential with the standard error of the regression coefficient errors calculated assuming the usual regression model. The 'mean' estimates are the unweighted means of the separate regression coefficients in each replicate, with the empirical standard error of this mean.

The realized heritabilities, with their empirical standard errors, are $11 \pm 1{\cdot}7\,\%$ and $18 \pm 3{\cdot}4\,\%$ for the upward and downward responses, respectively, and $15 \pm 2{\cdot}7\,\%$ for the divergence. These are within-family heritabilities, as selection was carried out within litters. There is no significant difference between the heritabilities calculated from the upward and downward response.

F lines

The results of 11 generations of selection for the ratio of gonadal fat pad weight to body weight in 10-week-old males are summarized in Figs. 3 and 4 and Tables

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Table 1. *Cumulative selection differentials* to generation 11 and phenotypic standard deviations*

Direction	Replicate 1	Replicate 2	Replicate 3	Mean	Phenotypic S.D.†
		A lines (adjusted food intake, g)			
High	37·8	35·6	38·4	37·3	
Low	−38·3	−37·1	−35·4	−36·9	
Control	0·5	2·4	0·2	1·0	5·20
		F lines (gonadal fat pad wt/body wt, mg/g)			
High	16·8	16·9	16·9	16·9	
Low	−11·4	−9·9	−10·8	−10·7	
Control	0·2	−0·9	3·1	0·8	4·09
		P lines (body wt −[8 × gonadal fat pad wt, g])			
High	12·4	10·3	11·3	11·3	
Low	−8·7	−8·6	−8·3	−8·5	
Control	−0·2	1·1	0·7	0·5	3·00

* Values for F and P halved, since selection only among males.
† Pooled within generations of the control.

Table 2. *Realized heritabilities* (%) (±S.E.) *to generation 11 for deviation of* high *from control, deviation of* low *from control and* divergence *between high and low*

	Replicate 1	Replicate 2	Replicate 3	Pooled*	Mean†
		A lines (adjusted food intake)			
High	14±4·5	8±4·2	11±7·1	11±4·5	11±1·7
Low	25±3·9	16±3·8	14±5·6	15±3·2	18±3·4
Divergence	20±2·5	11±2·8	13±3·4	14±2·2	15±2·7
		F lines (gonadal fat pad wt/body wt)			
High	34±4·4	50±6·8	28±12·7	37±5·8	37±6·5
Low	38±12·3	68±14·8	64±8·6	55±7·1	57±9·4
Divergence	35±5·5	55±6·6	41±5·9	43±3·4	44±5·9
		P lines (body wt −[8 × gonadal fat pad wt], g)			
High	75±9·1	38±9·0	50±9·2	56±7·5	54±10·9
Low	19±6·3	73±19·0	48±13·3	46±8·6	47±15·6
Divergence	52±6·3	53±4·9	49±6·0	54±3·5	51±1·2

* Pooled: regression of mean of lines on mean selection differential.
† Mean: arithmetic mean of regression coefficients with empirical S.E. from variance of regression between replicates.

1 and 2. As will be shown later, there is little difference between the high and low F lines in 10-week weight or in the index of fat-free mass, but large differences in the selected trait. The changes in the upward and downward direction were similar: the high lines increased by 36 %, and the low decreased by 44 % of the control value by generation 11, the total divergence of 80 % being about 2·8 phenotypic standard

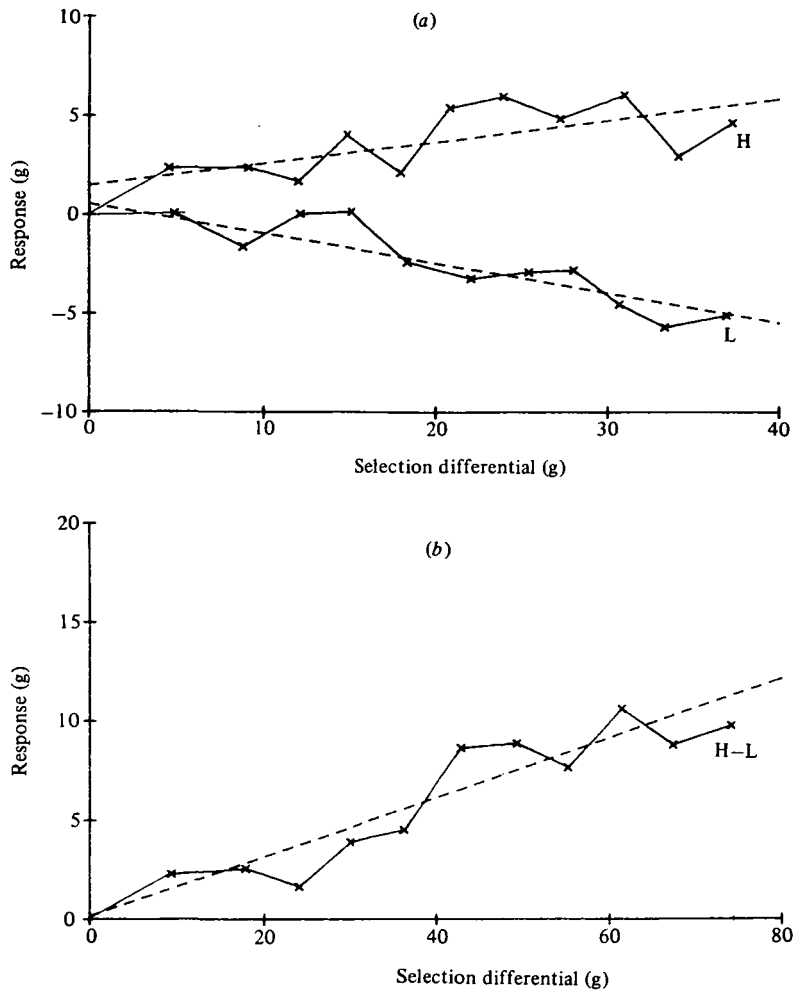

Fig. 2. A lines: mean response in adjusted food intake plotted against cumulated selection differential for (*a*) selected–control, (*b*) divergence (high–low).

deviations in the base population, even though selection was only in one sex. The high–low divergence is larger in replicates 1 and 2 than in replicate 3, being 83 %, 96 % and 61 % of the control values for replicates 1, 2, and 3, respectively.

The realized heritabilities, together with their standard errors, are $37 \pm 6{\cdot}5$ % and $57 \pm 9{\cdot}4$ % for the upward and downward responses respectively, and $44 \pm 5{\cdot}9$ % for the divergence. Although the heritability estimate is larger for the downward response than for the upward response, the difference is not significant. Selection differentials are smaller in the low lines, particularly in the later generations, because of the changes in variance associated with scale effects.

P lines

Figures 5 and 6 and Tables 1 and 2 summarize the results of selection for the index (body weight $-[8 \times$ gonadal fat pad weight] on 10-week-old males) which

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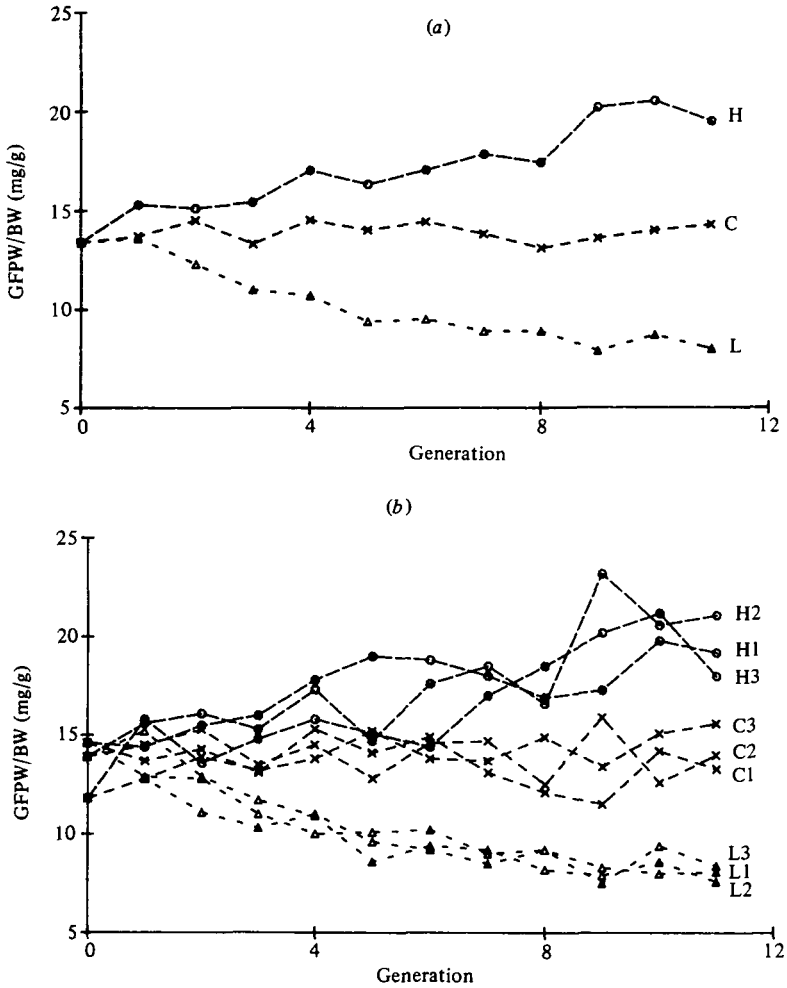

Fig. 3. F (fat) lines: ratio of gonadal fat pad weight to body weight (GFPW/BW) for (*a*) mean of all replicates, (*b*) individual replicates.

was constructed to estimate fat-free mass. There are large responses, mostly attributable to change in body weight. There is a marked difference in the selection responses in the upward and downward direction. By generation 11 the high lines have increased by 26·7 %, and the lows have decreased by 13·0 % of the controls, although much of this asymmetry can be attributed to the downward drift of the control line in replicate 1. There is little difference between the replicates in the high–low divergence at generation 11. The high–low differences as a proportion of the control mean equal 43 %, 34 % and 41 % for replicates 1, 2 and 3, averaging 40 % or 3·8 phenotypic standard deviations from selection on only one sex.

The realized heritabilities, with their standard errors, are $54 \pm 10{\cdot}9$ % and $47 \pm 15{\cdot}6$ % for the upward and downward responses respectively, and $51 \pm 1{\cdot}2$ % for the divergence. There is no significant difference between the heritabilities estimated from the upward and downward response.

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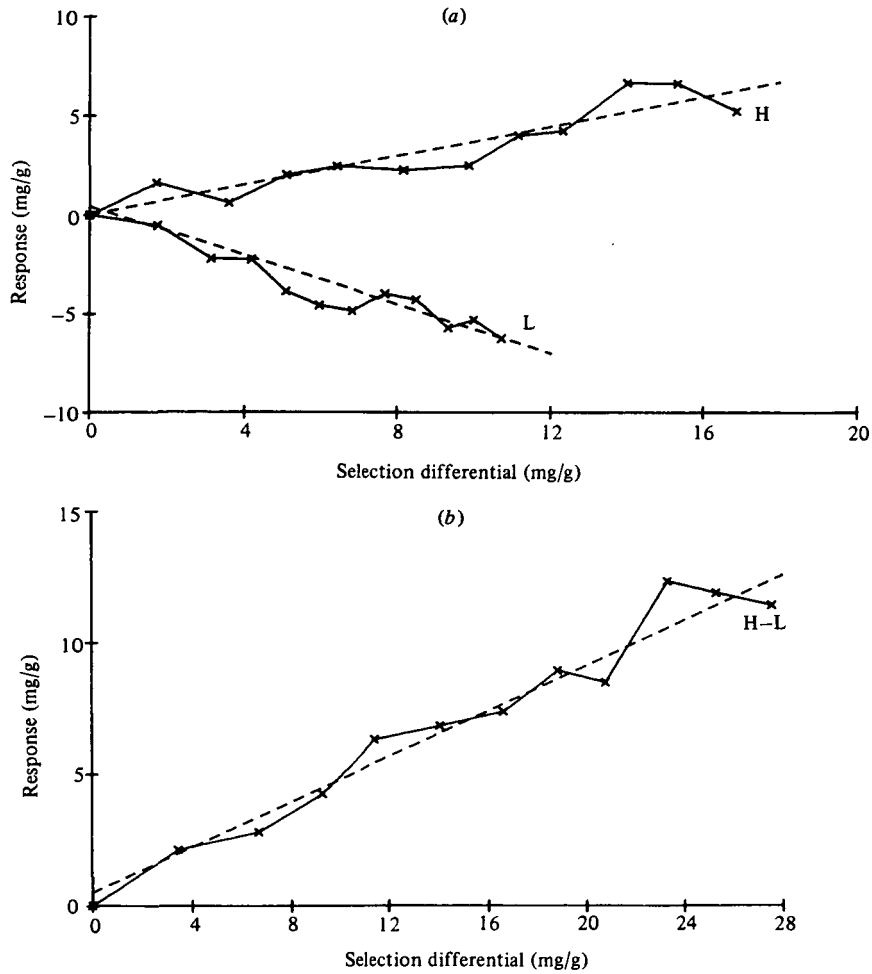

Fig. 4. F lines: mean response in the ratio of gonadal fat pad weight to body weight plotted against cumulated selection differential for (*a*) selected–control, (*b*) divergence (high–low).

(ii) *Correlated responses to selection*

Dissection of 10-week-old males

In generations 8 and 9 body weights and gonadal fat pad weights were recorded on 10-week-old males of all lines. Results, averaged over generations and replicates, are given in Table 3, together with significance tests based on the between-line variance after removing direction of selection and replicate effects.

The results show that the ratio of gonadal fat pad weight to body weight changed little in the P lines, the response in body weight being similar to that in the index. There were smaller, but significant responses in body weight in the A lines, with some indication that the high A lines were less fat than the low A lines. There was a small, non-significant response in body weight of the F lines, with the low being lighter although selected on a ratio which might be expected to favour high body weight.

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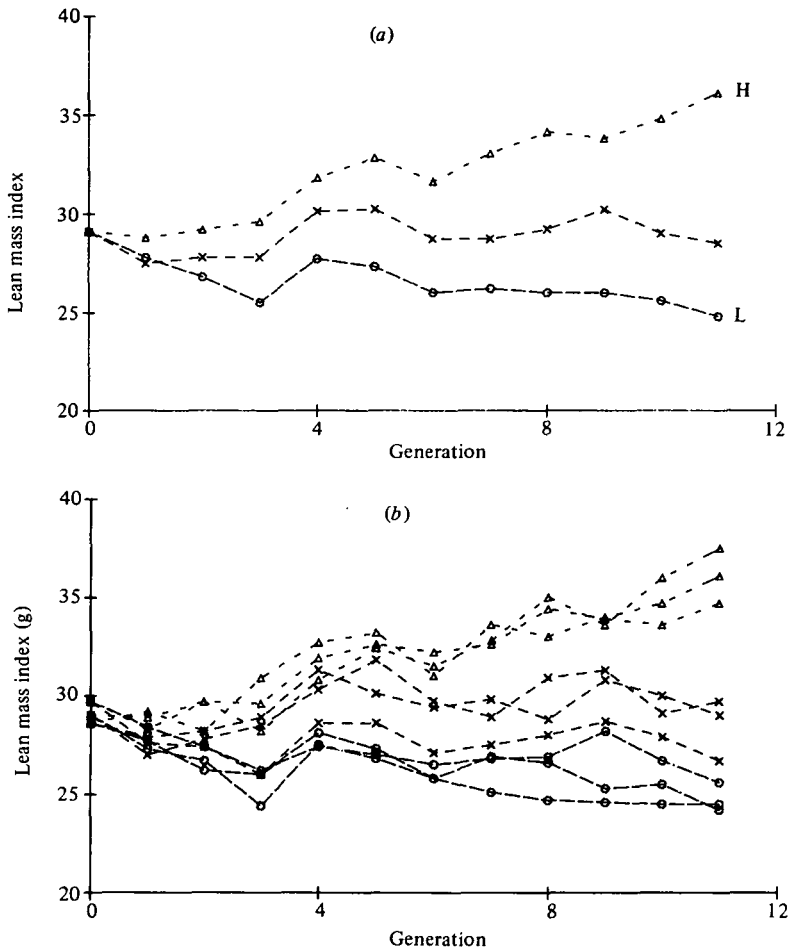

Fig. 5. P (protein) lines: index of lean mass (body weight $-[8 \times$ gonadal fat pad weight]) for (*a*) mean of all replicates, (*b*) individual replicates.

Body composition of 10-week-old males

In generation 7 chemical analysis was conducted on samples of 10-week-old males, and results are given in Table 4. The F lines differ substantially in whole body fat content, by about 4·2/11·7 or 36 % of the control value. This is, however, a smaller response than in the selection criterion of gonadal fat pad weight to body weight, about 64 % in generation 7, suggesting there has been some redistribution of fat. In the F lines the change in fat content has been accompanied by a complementary change in water content, but rather little in protein. As in the dissection data shown in Table 3, there is some indication that the low F lines are lighter.

Both the high A and high P lines have a lower fat percentage than their corresponding low lines; although not significant in both cases, they confirm results of Table 3. There is some indication of asymmetry, however. In terms of total protein weight, the high and low P lines diverge by some 1·29/5·92 or 22 %, the A lines diverge by 14 % and the F lines by very little.

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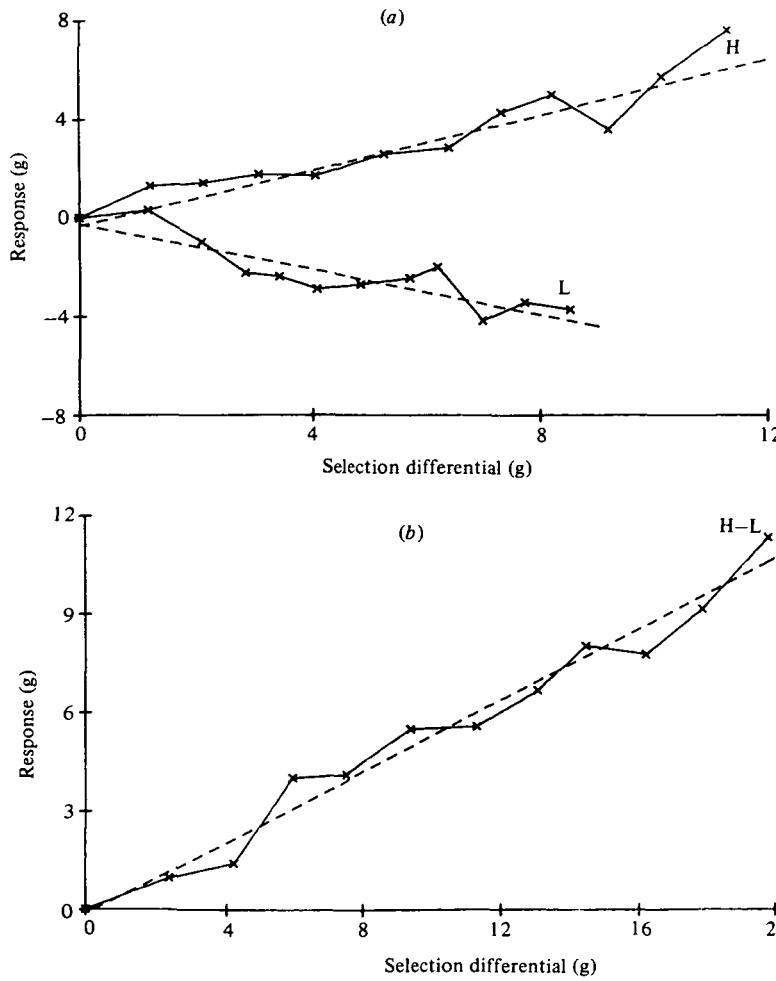

Fig. 6. P lines: mean response in the index of lean mass plotted against cumulated selection differential for (*a*) selected–control, (*b*) divergence (high–low).

Food intake

In generations 8 and 9 food intake from 4 to 6 weeks and body weights at these ages were recorded on samples of males and females of all lines. Results are summarized in Table 5. The high A, F and P lines are heavier than the corresponding low lines at both 4 and 6 weeks, with the divergence ranking P > A > F. Although the changes in 4-week weight were small in the A lines, these and data from each generation show that the simple phenotypic index did not prevent some response in 4-week weight. The A lines diverged more than the P lines in food intake, substantially more after adjustment for 4-week weight. In each of the A, P and F lines the increases in weight gain from 4 to 6 weeks were sufficient for food conversion efficiency (gain/food) to be higher for the high than for the low lines, but substantially and significantly so only in the P lines.

Table 3. *Dissection of 10-week-old males in generations 8 and 9: means of body weight (BW) and gonadal fat pad weight (GFPW) over replicates and significance tests. Standard errors and tests based on between-line variance*

Lines	No.	BW (g)	GFPW (mg)	GFPW/BW (mg/g)	BW-8GFPW (g)
		Means			
A (adjusted food intake)					
High	171	36·5	450	12·9	32·9
Control	92	34·4	532	15·5	30·2
Low	165	32·4	490	15·0	28·5
F (gonadal fat pad wt/body wt)					
High	159	33·2	634	18·7	28·2
Control	92	33·9	459	13·4	30·2
Low	176	31·5	264	8·4	29·3
P (body wt $-[8\times$ gonadal fat pad wt])					
High	163	38·0	505	13·3	34·0
Control	87	33·4	456	13·6	29·8
Low	167	29·3	410	13·8	26·0
S.E.		0·57	25·5	0·83	0·61
		Significance tests			
A					
H−L		**	—	—	**
(H+L)/2−C		—	—	—	—
F					
H−L		—	**	**	—
(H+L)/2−C		—	—	—	—
P					
H−L		**	*	—	**
(H+L)/2−C		—	—	—	—

** $P < 0{\cdot}01$; * $P < 0{\cdot}05$; — $P > 0{\cdot}05$.

Realized genetic correlations and heritabilities

A summary of the responses at generations 8 and 9 (from Tables 3 and 5) in those traits under direct selection in one or other line is given in Fig. 7. From these results genetic correlations were computed from

$$r = [(CR_{XY}\,CR_{YX})/(R_{XX}\,R_{YY})]^{\frac{1}{2}},$$

where, for example, R_{XX} and CR_{XY} are the direct and correlated responses in traits X and Y, respectively, from divergent selection in trait X (Table 6). In addition, values of full sib intra-class correlation (t) from analyses within line are given in Table 6 and from these predicted realized heritabilities (h^2) from mass selection computed using the formula $h^2 = 2(1-t)h_w^2$, where h_w^2 is the within-family realized heritability (from Table 2).

The genetic correlation between the selection criteria of the A and P lines is around 0·5, that among the other criteria is small. Because the full sib intra-class correlations are near 0·5, the heritabilities from mass selection are predicted to be similar to those realized from within-family selection.

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Table 4. *Body composition of 10-week-old males in generation 7: means over replicates (48 mice) and significance tests. Standard errors and tests based on between-line variance*

Lines	Water (%)	Ash (%)	Fat (%)	Protein (%)	Body wt (g)	Fat (g)	Protein (g)	Energy (kJ)	Energy /BW (kJ/g)
					Means				
A (adjusted food intake)									
High	66·7	3·27	10·5	19·5	34·2	3·61	6·67	72·0	2·11
Control	65·0	3·46	11·7	19·9	31·2	3·63	6·21	69·6	2·23
Low	65·8	3·42	11·5	19·3	30·2	3·46	5·81	65·7	2·18
F (gonadal fat pad wt/body wt)									
High	63·8	3·29	13·7	19·2	30·3	4·15	5·80	72·2	2·39
Control	65·2	3·44	11·7	19·6	30·5	3·57	5·98	67·7	2·22
Low	66·9	3·46	9·5	19·6	28·9	2·73	5·67	58·0	2·01
P (body wt $-[8\times$ gonadal fat pad wt])									
High	65·3	3·58	11·6	19·5	34·8	4·04	6·79	76·7	2·21
Control	64·9	3·53	11·5	20·1	29·4	3·39	5·92	65·7	2·23
Low	64·0	3·58	12·8	19·5	28·2	3·62	5·50	65·5	2·32
S.E.	0·33	0·066	0·30	0·22	0·50	0·143	0·116	1·83	0·029
					Significance tests				
A									
H − L	—	—	—	—	**	—	**	*	—
(H + L)/2 − C	**	—	—	—	—	—	—	—	*
F									
H − L	**	—	**	—	—	**	—	**	**
(H + L)/2 − C	—	—	—	—	—	—	—	—	—
P									
H − L	*	—	*	—	**	—	**	**	*
(H + L)/2 − C	—	—	—	*	**	*	—	*	—

** $P < 0{\cdot}01$; * $P < 0{\cdot}05$; — $P > 0{\cdot}05$.

4. DISCUSSION

Selection for increased food intake has previously been carried out in mice (Sutherland *et al.* 1970) and in chickens (Pym & Solvyns, 1979). Sutherland *et al.* found the realized heritability of 4- to 11-week food intake to be $0{\cdot}20 \pm 0{\cdot}057$, which is not greatly different from the realized (within-litter) heritability estimate of $0{\cdot}15 \pm 0{\cdot}027$ obtained in this study for 4- to 6-week food intake, adjusted for 4-week weight. It is possible that the adjustment for 4-week weight removes some of the genetic variability of 4- to 6-week food intake, and therefore reduces the heritability. Some indication of this was obtained from an offspring–parent regression analysis, performed from data on 10 generations of the A control lines (which were the only unselected populations on which food intake was regularly recorded), which gave estimates of $-0{\cdot}02 \pm 0{\cdot}078$ and $0{\cdot}17 \pm 0{\cdot}075$ for the heritability of adjusted and

Table 5. *Food intake trials in generations 8 and 9, means over replicates and significance tests. Standard errors and tests based on between-line variance*

Line	No.	Adj. food† intake (g)	Food intake (g)	4-week wt (g)	6-week wt (g)	Efficiency (gain/food) (%)
			Means			
A (adjusted food intake)						
High	327	67·1	69·9	18·8	27·5	12·4
Control	175	61·3	63·5	18·1	25·1	11·1
Low	292	57·8	57·8	17·5	24·0	10·8
F (gonadal fat pad wt/body wt)						
High	290	59·2	59·4	17·1	25·0	13·5
Control	164	59·5	59·6	16·9	24·1	13·4
Low	316	58·5	57·6	16·6	23·8	12·4
P (body wt −[8 × gonadal fat pad wt])						
High	320	62·8	65·4	18·6	28·3	15·2
Control	155	60·1	59·2	16·6	24·9	14·0
Low	307	58·0	55·0	16·4	21·8	11·9
S.E.		0·73	0·92	0·47	0·48	0·49
			Significance tests			
A						
H−L		**	**	—	**	—
(H+L)/2−C		—	—	—	—	—
F						
H−L		—	—	—	—	—
(H+L)/2−C		—	—	—	—	—
P						
H−L		**	**	**	**	**
(H+L)/2−C		—	—	—	—	—

† Adjusted food intake: food intake adjusted for 4-week weight by within-litter and sex regression.

** $P < 0{\cdot}01$; — $P > 0{\cdot}05$.

unadjusted food intake, respectively. Although the realized heritability of adjusted food intake was higher than this, the analysis suggests that that of unadjusted intake would have been even higher.

Both Sutherland *et al.* and Pym & Solvyns found that their selected animals became fatter than unselected controls, but in this study the mice selected for increased food intake became leaner than the controls. This difference could be a consequence of the adjustment of food intake for 4-week weight in this experiment. Animals that eat the most will normally be those that are heaviest at the start of the test period, but if differences in body weight are taken into account, the animals that eat most may be those that are leanest and therefore have fewest energy reserves. The decrease in fatness in high A-line mice in this study might explain their increased gross efficiency, as it is more efficient to lay down lean in terms of gain in g/intake but not in terms of gain in kJ/intake (Pullar & Webster, 1977). Sutherland *et al.* found no change in gross efficiency in their selected mice, and the chickens selected by Pym and Solvyns decreased in gross efficiency.

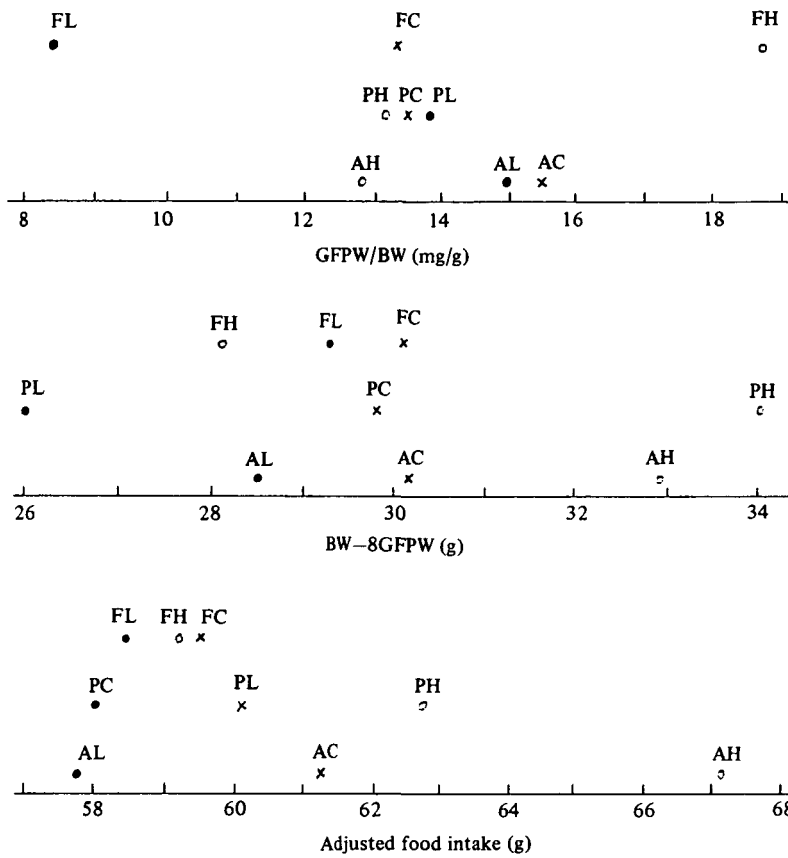

Fig. 7. Mean values for the indices used as selection criteria for the nine sets of lines, averaged over replicates and over generations 8 and 9.

Table 6. *Realized genetic correlations* (r), *intra-class correlations of full sibs* (t) *and predicted heritabilities from mass selection* (h^2)

	r			
	GFPW/BW	BW-8GFPW	t	h^2
Adjusted food intake	—†	0·53	0·43	0·17
Predicted fat proportion (GFPW/BW)		0·12	0·43	0·50
Predicted lean mass (BW-8GFPW)			0·48	0·50

† No estimate computed: correlated responses small but of opposite sign.

Further analysis by M. Nielsen (unpublished) confirms the increased leanness of the high A lines using chemical analysis of whole animals at 4 and 6 weeks of age, and will provide data on the maintenance requirement and the energetic efficiency of mice from all the lines. These results should lead to a better understanding of the changes in gross efficiency, food intake and body composition that have occurred in the A lines.

Selection for the ratio of gonadal fat pad weight to body weight in the F lines has produced significant differences in percentage total carcass fat. The changes in the percentage of fat have been accompanied by changes in the opposite direction in that of water, but no significant change in that of protein. The ratio of gonadal fat pad weight to body weight as an estimator of total percentage fat has limitations. In generation 7, the high–low difference in total fat, as a proportion of the control mean, was 36 %, compared with a difference in the ratio of gonadal fat pad weight to body weight of 64 %.

McCarthy & Doolittle (1977) selected mice for 10-week weight and obtained a realized (within-litter) heritability of $0{\cdot}33 \pm 0{\cdot}020$. This is lower than the estimate of $0{\cdot}51 \pm 0{\cdot}012$ obtained in this study for the realized heritability of the index (10-week body weight $-[8 \times$ gonadal fat pad weight]). From an offspring–parent regression analysis of data from the F and P control lines, the heritabilities of 10-week weight and the index (10-week body weight $-[8 \times$ gonadal fat pad weight]) were estimated to be $0{\cdot}35 \pm 0{\cdot}071$ and $0{\cdot}29 \pm 0{\cdot}070$, respectively.

Mice that are selected for increased body weight or weight gain generally increase in food intake and gross efficiency (Timon, Eisen & Leatherwood, 1970; Fowler, 1962; Roberts, 1981) and in percentage fat (Robinson & Bradford, 1969; McPhee & Neill, 1976; Hayes & McCarthy, 1976; Hull, 1960), although increases in fatness are smaller when selection is carried out at a later age. The index used in the selection of the P lines (body weight $-[8 \times$ gonadal fat pad weight]) was designed to maximize change in body weight without a change in carcass fat. It is, however, very highly correlated with body weight. Although the P low lines were fatter at generation 7, in later generations there was little difference in fatness between the lines. The P high line mice increased in both food intake and gross efficiency.

Overall, the experimental design has enabled us to achieve our aim of producing by selection differences between lines in appetite, fat percentage and lean gain, which are repeatable as shown by the replication. Further experiments on the lines of mice will include measurements of body weights and food intake at later ages, maintenance requirements and energetic efficiency, and rates of protein turnover. There are large differences in litter size between the high and low A lines, which are currently being investigated. These will be discussed in a later paper.

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