Theor Appl Genet (1992) 83:973–980

Restricted index selection in mice designed to change body fat without changing body weight: direct responses*

E. J. Eisen

Department of Animal Science, Box 7621, North Carolina State University, Raleigh, NC 27695, USA

Received September 18, 1991; Accepted November 1, 1991
Communicated by G. Wenzel

Summary. Replicated within full-sib family restricted index selection was conducted for eight generations in mice for high or low epididymal fat pad weight (EF) holding body weight (BW) constant. Pooled realized heritability estimates of index units based on high, low and divergent selection were 0.42 ± 0.20, 0.44 ± 0.19 and 0.42 ± 0.05, respectively, which were not different from the base population estimate of 0.33 ± 0.10. Realized responses per generation pooled across replicates in the high-fat restricted index lines were in the expected directions for EF (17.5 ± 7.2 mg; $P < 0.05$) and BW (0.03 ± 0.58 g; $P > 0.05$), but responses in the low-fat restricted index lines were discrepant for EF (0.3 ± 5.1 mg; $P > 0.05$) and BW (0.38 ± 0.01 g; $P < 0.01$). Consequently, the realized responses in component traits were decidedly asymmetric ($P < 0.05$). A technique for estimating realized genetic parameters from index selection lines gave realized heritabilities for BW and EF of 0.68 ± 0.04 and 0.45 ± 0.05, respectively, and a realized genetic correlation between BW and EF of 0.93 ± 0.01 compared with base population estimates of 0.43 ± 0.08, 0.49 ± 0.10 and 0.78 ± 0.05, respectively. Possible explanations for the disparity between observed and expected responses in the low-fat restricted index lines include genetic drift, poor estimates of base population parameters, changes in genetic parameters with selection, linkage disequilibrium resulting from selection and asymmetric realized relative index weights.

Key words: Mice – Fat – Selection index – Heritability – Genetic correlation

Introduction

A primary goal of livestock breeding programs generally includes simultaneous genetic improvement of multiple traits. The selection index is recognized as the most efficient method to accomplish this objective (Young 1961). Often the desired direction of selection for two traits that are to be improved with the use of an index conflict with the sign of the genetic correlation between the traits, a situation known as antagonistic index selection (Rutledge et al. 1973; Nordskog et al. 1974). An example of two such traits is body fat and body weight or growth rate. In many countries there is an economic incentive to select for reduced fat content while at the same time increasing growth rate. Yet in pigs backfat depth and growth rate are positively genetically correlated (Biswas et al. 1966; Stewart and Schinckel 1990), and in poultry there is a positive genetic correlation between abdominal fat and body weight (Leenstra and Pit 1988). An analogous situation exists in mice, which are widely used as a model for livestock to study complex quantitative traits (Falconer 1989; Eisen 1989), where there exists a positive genetic correlation between body weight and each fat depot (Eisen and Prasetyo 1988).

The objective of the present study was to determine the efficacy of using a restricted selection index in mice to select antagonistically for high or low body fat content with no accompanying change in body weight. These lines will provide valuable models for studying the genetics of maintenance requirements and the partial efficiencies of fat and protein deposition (Eisen 1989). A com-

---

* The research reported in this publication was funded by the North Carolina Agricultural Research Service (NCARS), Raleigh, NC 27695-7643, USA. The use of trade names in this publication does not imply endorsement by the NCARS, nor criticism of similar ones not mentioned

panion paper presents the results of a suite of correlated traits (Eisen 1992).

Materials and methods

Formation of base population

The base population of mice used in this study was formed by reciprocally crossing two replicate control lines (RC1, RC2) that were used in a single-trait selection experiment designed to alter components of body composition (Eisen 1987). The composite population was randomly mated with approximately 75 sire-dam pairs per generation for two generations to reduce linkage disequilibrium prior to initiation of selection.

Selection procedures

Each line was maintained with 15 pair-matings per generation. Three reserve matings were available from each line in case replacements were required because of infertility or mortality. Selection was conducted within full-sib families to minimize inbreeding and maternal effects. Pair-matings were made at random with the avoidance of sib matings. The expected effective population size in each line was approximately 60.

Weight of the right epididymal fat pad (EF) was used as an indicator trait of total body fat weight because the two traits are phenotypically highly correlated. Estimates of phenotypic correlations between EF and body fat excluding EF were 0.86, 0.81, 0.86, 0.90 and 0.96 at 4, 6, 10, 16 and 30 weeks of age, respectively (Eisen and Leatherwood 1978).

Restricted index selection was conducted for high or low 12-week EF while holding 12-week body weight (BW) unchanged in two replicates for eight consecutive generations. Replicate high and low index lines are designated HE1, HE2 and LE1, LE2, respectively, and replicate control lines are referred to as RS1, RS2. Omission of the replicate number, e.g. HE, indicates pooling of lines.

The restricted selection index was first developed by Kempthorne and Nordskog (1959). Extension of the restricted index to within-family selection does not affect the solution to the equations for the relative index weights, but it is important to note that within full-sib family phenotypic and additive genetic variance-covariance matrices were used to obtain solutions. Estimates of genetic and phenotypic parameters used to calculate index weights are given in Table 1. The restricted selection index was found to be $I = 11.93\ P_{BW} - 0.3323\ P_{EF}$, where P_{BW} and P_{EF} are phenotypic values for 12-week body weight and epididymal fat pad weight, respectively. The index is defined so that an increase in index units results in a decrease in EF and vice versa.

Expected response in the vector of component traits in the index was determined as $\Delta = kG'b/(b'Pb)^{\frac{1}{2}}$, and the heritability of index units was calculated as $h^2 = b'Gb/b'Pb$ (Eisen 1977; Lin and Allaire 1977; Nordskog 1978), where $\Delta = 2 \times 1$ vector of responses in BW and EF, k = selection intensity, G and P are 2×2 additive genetic and phenotypic variance-covariance matrices, respectively, involving BW and EF, and $b' = 1 \times 2$ vector of weights applied in the index (11.93–0.3323).

Table 1. Estimates of phenotypic and genetic parameters used to develop the restricted selection index

Trait[b]	V_A	V_p	h^2	t
BW (g)	6.37	14.82	0.43 ± 0.08[c]	0.35 ± 0.04
EF (mg)	13,502.44	27,556.00	0.49 ± 0.10	0.28 ± 0.04

Traits	$C_{A_{BW}A_{EF}}$	$C_{P_{BW}P_{EF}}$	$r_{G_{BW,EF}}$	$r_{P_{BW,EF}}$	$t_{BW,EF}$
BW, EF	228.75	428.20	0.78 ± 0.05	0.67	0.20

[a] From data of Eisen and Prasetyo (1988). Heritabilities and genetic correlations were estimated by son-sire regressions

[b] BW, 12-week body wt; EF, 12-week epididymal fat pad wt; V_A and V_p are additive genetic and phenotypic variances; h^2, heritability; t, intraclass correlation between full sibs; $C_{A_iA_j}$ and $C_{p_ip_j}$ are additive genetic and phenotypic covariances, respectively; $r_{G_{BW,EF}}$ and $r_{P_{BW,EF}}$ are genetic and phenotypic correlations, respectively; $t_{BW,EF}$ is covariance of full-sibs divided by the geometric mean of the phenotypic variances

[c] Standard errors

In each generation, 60 approximately 9-week-old male-female pairs in the selected lines and 30 pairs in the controls were cohabited for 16 days, during which time they were fed ad libitum Purina Laboratory Chow 5001 (Purina Mills, Richmond, Ind.). Males represented progeny from 15 full-sib families, with a mean of four full-brothers per family in selected lines and two in control lines. Following the period of cohabitation, males were continued on the same diet and were caged singly until 12 weeks of age when they were weighed and killed by cervical dislocation. The right epididymal fat pad was dissected and weighed. Based on the selection criterion within each line, one male was selected within each of the 15 full-sib families. If a selected male could not be used because of infertility, litter mortality or insufficient male progeny, then a reserve male was selected.

Females were fed ad libitum Purina Mouse Chow 5015 from the time they were separated from their mate until their litter was weaned. Litters were standardized randomly within gender to ten pups at 1 day of age, attempting to obtain an equal sex ratio. Foster pups in augmented litters were identified by clipping their tail and were discarded at weaning.

Statistical analysis

Primary selection differentials for index units and secondary selection differentials for BW and EF were calculated as the mean of the deviation of each selected male from its full-sib family mean and then halved because it was assumed that selection was applied to male parents only. Preliminary analysis indicated that unweighted selection differentials did not differ from selection differentials weighted by the number of progeny of each male measured for the selected traits in the next generation, so that only the former was used. Realized index weights were calculated using the procedure described by Dickerson et al. (1954) modified by using the within full-sib family phenotypic variance-covariance matrix.

Direct and correlated responses were estimated as the regressions of selected line means, deviated from control line means each generation to account for environmental effects, on generation number. Realized heritabilities of index units were estimated as the regressions of generation mean responses on cumulative selection differentials. Responses and realized heritabilities also were based on divergence between high and low index lines (HE–LE) (Falconer 1989). Tests of asymmetry of responses were based on the contrast HE + LE – 2RS. Hill (1972a, b) has shown that the least-squares estimates of realized heritabilities and responses are unbiased, but that the least-squares standard errors are biased downward. Therefore, empirical standard errors were estimated from the variation between replicates.

Because the realized heritability of index units (h_R^2) was based on within full-sib family selection, individual heritability of index units was calculated as $h^2 = h^2_R\ (1-t)/(1-r)$, where t = estimated intraclass correlation among full-sibs for index units and $r = \frac{1}{2}$ = Wright's relationship coefficient between full-sibs. The estimate of t for index units was 0.28 ± 0.04 using data from Eisen and Prasetyo (1988).

Realized heritabilities of and realized genetic correlations between the component traits of the index were estimated by modifying procedures outlined by Harvey (1972), Rutledge et al. (1973) and Berger and Harvey (1975) to take into account within-family selection. Realized genetic correlations between index units and component traits were based on the following formula (Rutledge et al. 1973):

$$r_G = b_{G_{ij}}\ (h^2_j\ V_{P_j} / h^2_i\ V_{P_i})^{1/2}$$

where $b_{G_{ij}}$ is the realized regression of the unselected trait on the selected trait, h^2_j and h^2_i are heritabilities, and V_{P_j} and V_{P_i} are phenotypic variances of the selected and unselected traits. Heritabilities were obtained from the realized estimates described above, and phenotypic variances were obtained from each replicate line pooled within generations.

Results

Control lines

Base population means, phenotypic standard deviations and coefficients of variation for index units, 12-week body weight and 12-week epididymal fat pad weight were estimated by pooling generation data from RS1 and RS2 (Table 2). Variation in EF was considerably larger than in BW. Mean and variation in BW were similar to values estimated in RC1 and RC2, the progenitor lines, while mean and variation in EF were much lower (Eisen 1987). Slopes of generation means on generation number for index units and component traits were not different from zero ($P > 0.05$) in the control lines (Table 2).

Selection differentials

Absolute values of the primary cumulative selection differentials in index units were larger in HE than in LE (Table 3). Secondary cumulative selection differentials for BW were lower in absolute value in HE than in LE, but the reverse was true for EF. This result is reflected in the lower realized relative index weights (RRIW) applied to BW in the HE replicates compared to the LE replicates (Table 3). RRIW in HE were lower than intended; in LE they were higher than intended. In general, replicates within HE and LE responded similarly in RRIW.

Selection responses and realized heritabilities of index units

Responses in index units are plotted in Fig. 1 as deviations from control line means each generation and in Fig. 2 as divergence between HE and LE. Pooled responses in index units (Table 4) were significant in HE ($P < 0.05$) and LE ($P < 0.05$) and for divergence, with no evidence of asymmetry ($P > 0.05$).

Table 2. Base population means, phenotypic standard deviations ($\sqrt{V_p}$), coefficients of variation (CV) and regressions of generation means on generation number ± standard errors (b ± SE)

Trait[a]	Mean[b]	$\sqrt{V_p}$[b]	CV[b]	b ± SE[c]
I	354	37.75	106.64	0.66 ± 1.27
BW (g)	37.9	3.51	9.25	−0.11 ± 0.16
EF (mg)	295	112.27	38.06	−5.8 ± 4.5

[a] I, Index units; BW, 12-week body wt; EF, 12-week epididymal fat pad wt

[b] Pooled within replicate controls (RS1, RS2) and generations (n = 1,068)

[c] Pooled within replicate controls

Table 3. Primary (index units) and secondary (BW, EF) cumulative selection differentials (CSD) and realized relative index weights (RRIW)

Line	CSD[c]			RRIW[d]	
	I[b]	BW (g)	EF (mg)	BW	EF
HE1	−155.01	−3.37	345.76	26.21	−1
HE2	−174.70	−2.09	447.98	27.23	−1
LE1	136.61	8.15	−118.83	49.31	−1
LE2	115.85	6.03	−132.61	46.65	−1
Intended[a]				35.90	−1

[a] Based on restricted selection index applied in the selection experiment

[b] See footnote a in Table 2 for definition of traits

[c] Values are halved because selection is only on males

[d] Calculated by the method of Dickerson et al. (1954) using within-family phenotypic variance-covariance matrix and secondary cumulative selection differentials

Table 4. Regression coefficients ± SE of responses on generation number

Line	Trait[c]		
	I	BW, g	EF, mg
HE1[a]	−7.95 ± 1.77**	−0.38 ± 0.16*	10.3 ± 6.9
HE2[a]	−3.00 ± 1.77[+]	0.44 ± 0.16*	24.7 ± 6.9**
Pooled[b]	−5.48 ± 2.48*	0.03 ± 0.58	17.5 ± 7.2*
LE1[a]	2.66 ± 1.77	0.37 ± 0.16*	5.4 ± 6.9
LE2[a]	6.14 ± 1.77**	0.39 ± 0.16*	−4.7 ± 6.9
Pooled[b]	4.40 ± 1.74*	0.38 ± 0.01**	0.3 ± 5.1
Divergence1[a]	−10.61 ± 1.91**	−0.75 ± 0.16**	4.9 ± 5.2
Divergence2[a]	−9.15 ± 1.91**	0.05 ± 0.16	29.4 ± 5.2**
Pooled[b]	−9.88 ± 0.73**	−0.35 ± 0.40	17.2 ± 12.2
Asymmetry[a]	1.08 ± 2.44	0.41 ± 0.24*	17.8 ± 8.5*

[a] Standard errors estimated by least-squares

[b] Standard errors estimated from variance between replicates

[c] See footnote a in Table 2 for definition of traits

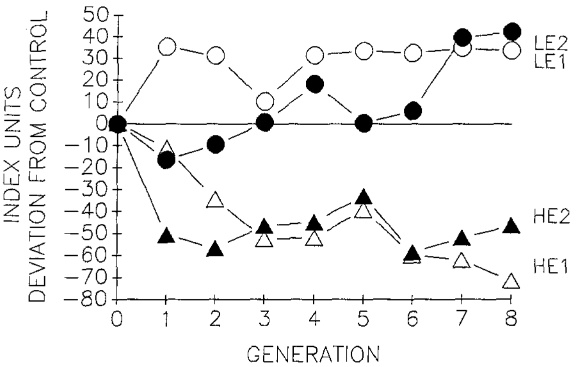

Fig. 1. Generation mean responses in index units in HE and LE lines as deviations from control line means

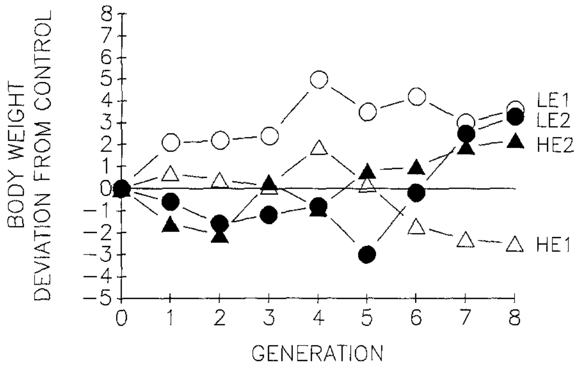

Fig. 3. Generation mean responses in BW (body weight) in HE and LE lines as deviations from control line means

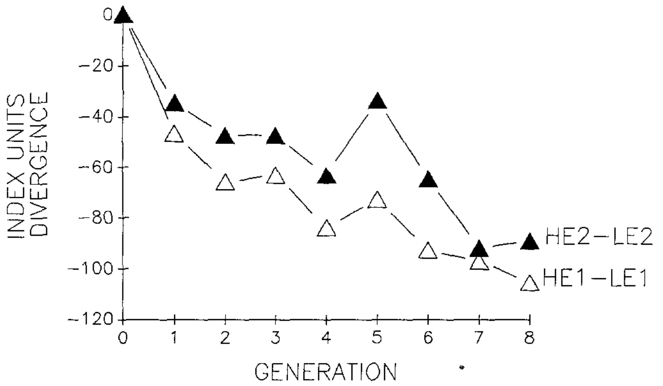

Fig. 2. Generation mean responses in index units as HE-LE divergence

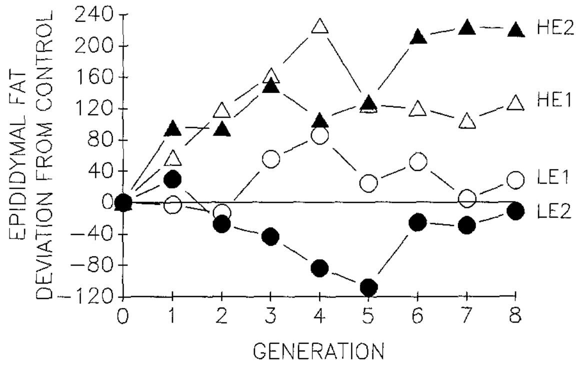

Fig. 4. Generation mean responses in EF (epididymal fat) in HE and LE lines as deviations from control line means

Realized heritability estimates for index units (h_R^2) varied considerably between replicates in high and low selected lines, but pooled realized heritabilities were similar for both directions of selection and for divergence (Table 5). Pooled realized heritabilities, converted to an individual basis, were similar for HE, LE and divergence and were not significantly different from the heritability of index units estimated from base population son-sire regression (Eisen and Prasetyo 1988).

Selection responses and realized parameters in component traits

Regression coefficients of generation mean responses (Fig. 3, 4) on generation number in the component traits of the restricted selection index are presented in Table 4. The pooled response to selection in HE was positive for EF and nearly zero for BW, but there was considerable replicate variation. Contrary to expectation, the response in LE was negligible for EF and positive for BW. Asymmetry in responses was found for both EF and BW.

These observed responses can be compared with expected responses. Based on selecting one out of four males within each family, the expected selection intensity is 1.029 (Becker 1984), which is halved because it was assumed that no selection was applied to males. Using the selection intensity of 0.514 and base population statistics, the expected responses per generation to within-family selection for the component traits were found to be zero for BW and ±11.4 mg for EF. Therefore, the realized responses in HE were in fair agreement with expectation, but the realized responses in LE were clearly discrepant.

Realized genetic correlations between index units and component traits are presented in Table 6. Based on the results of responses in component traits, one would predict good agreement between expected and observed estimates in HE but not in LE. Based on the genetic parameter estimates used to construct the restricted selection index, the expected genetic correlation between index units and BW was found to be zero and the genetic correlation between index units and EF was −0.63. Pooled realized genetic correlations in the HE line were not different from expectation (Table 6). However, as expected, the realized genetic correlations for BW and EF in the LE line were not in agreement with predicted values. Estimates from divergence fluctuated widely and were intermediate between HE and LE.

Table 5. Realized heritability estimates (h_R^2) ±SE for index units

Line	$h_R^2 \pm SE$	$h^2 \pm SE^d$
HE1[a]	0.44±0.10	0.63±0.14
HE2[a]	0.15±0.08	0.22±0.12
Pooled[b]	0.30±0.14	0.42±0.20
LE1[a]	0.18±0.11	0.26±0.16
LE2[a]	0.43±0.13	0.62±0.19
Pooled[b]	0.31±0.13	0.44±0.19
Divergence1[a]	0.31±0.05	0.45±0.07
Divergence2[a]	0.26±0.05	0.37±0.07
Pooled[b]	0.29±0.03	0.42±0.05
Son-sire regression[c]		0.33±0.10

[a] Standard errors estimated by least-squares

[b] Standard errors estimated from variance between replicates

[c] Estimated from data of Eisen and Prasetyo (1988)

[d] Individual heritability = $h^2 = h_R^2 (1-t)/(1-r)$ where h_R^2 = realized heritability based on within full-sib family selection, and t = intraclass correlation between full-sibs and r = Wright's relationship between full-sibs

Table 6. Realized genetic correlations between index units and component traits ($r_{GI,BW}$; $r_{GI,EF}$) ±SE[a]

Line	$r_{GI,BW}$	$r_{GI,EF}$
HE1	0.37	−0.69
HE2	0.03	−0.51
Pooled	0.20±0.17[b]	−0.60±0.09
LE1	0.52	−0.05
LE2	0.73	−0.09
Pooled	0.62±0.11	−0.07±0.02
Divergence1	0.55	−0.30
Divergence2	0.14	−0.60
Pooled	0.35±0.21	−0.45±0.15

[a] See footnote a in Table 2 for definition of traits

[b] Standard errors are estimated from variation between replicates

Table 7. Realized heritabilities of and genetic correlation between BW and EF estimated simultaneously from the two restricted index lines[a]

Estimate[b]	$h^2_{BW} \pm SE$	$h^2_{EF} \pm SE$	$r_{GBW,EF} \pm SE$
Rep 1[c]	0.72±0.05	0.40±0.01	0.93±0.03
Rep 2[c]	0.65±0.05	0.50±0.01	0.93±0.03
Pooled[d]	0.68±0.04	0.45±0.05	0.93±0.01

[a] See footnote b in Table 1 for definition of terms

[b] Rep 1 results are based on responses in HE1, LE1, and Rep 2 results are based on responses in HE2, LE2

[c] Standard errors estimated by least-squares

[d] Standard errors estimated from variance between replicates

Results of simultaneously estimating realized genetic parameters of component traits from the pair of restricted selection index lines are presented in Table 7. Estimates from both replicates were in good agreement. The pooled realized heritability for BW and the pooled realized genetic correlation between BW and EF were significantly larger than the base population estimates (Table 1), while the realized and base population estimates of heritability for EF were similar.

Discussion

Eight generations of replicated within full-sib family restricted index selection for high or low epididymal fat pad weight, holding body weight unchanged, resulted in responses and realized heritabilities that were symmetric and in good agreement with base population parameters. Realized individual heritability based on divergence was 0.42±0.05. However, when component traits of the restricted index were examined, asymmetry of responses was apparent. Selection responses for high EF with no change in BW were in good agreement with theoretical expected values although variation between replicates was sizable. In contrast, selection for low EF, holding BW unchanged, actually resulted in responses opposite to expectation, i.e., no change in EF and an increase in BW. The responses in the LE line provided an example of how the overall index units can agree with expectation, but the component traits can fail to do so.

Campo and Velasco (1989) have reviewed the literature on antagonistic index selection for two traits under different types of selection: (1) restricted selection with a genetic correlation either greater than or less than zero; (2) selection in opposite directions for two traits with a positive genetic correlation; and (3) selection in the same direction for two negatively correlated traits. They indicated that many antagonistic index selection experiments found discrepancies between observed and expected responses. In the case of restricted indices, most often selection response in the unrestricted trait is less than expected, whereas response in the restricted trait is greater than zero.

Two other restricted selection index experiments have been reported in mice. Restricted index selection for increased or decreased postweaning gain holding change in feed intake to zero resulted in realized responses that were in agreement with expectations for postweaning gain, but feed intake changed in the direction of response in postweaning gain after the first few generations of selection (Eisen 1977). McCarthy and Doolittle (1977) used a restricted selection index intended to increase or decrease body weight at 5 weeks of age while holding body weight constant at 10 weeks of age, and vice versa, so that all four combinations of high and low selection and 5 and 10 week restrictions were considered. While restricted index selection was generally successful, realized responses did not agree very well with predicted responses; specifically, expected responses of zero were never realized. Abplanalp et al. (1963) used a restricted selection index in turkeys designed to increase 8-week body weight while holding 24-week body weight constant. The restricted index was moderately successful, although body weight at 24 weeks responded downward.

None of these three experiments was replicated, so it is possible that genetic drift may have contributed to discrepancies between observed and expected responses (Hill 1972a, b). Campo et al. (1990) concluded that discrepancies between observed and expected responses in index selection studies with *Tribolium* may be associated with genetic drift. In fact, genetic drift may be responsible for disparate results in the present study because the use of only two replicates may not provide an adequate empirical estimate of the variance of response. However, the effective population size of 60 in each replicate line should have adequately minimized drift and inbreeding effects.

Sharp et al. (1984) selected replicate lines of mice for high or low lean body mass based on the phenotypic index I = BW − (4)(2) EF. The rationale for this index was based on the fact that the pair of epidymal fat pads represent about one-eighth of total fat in 10-week-old males; therefore, the lean index would be a suitable predictor of fat-free mass. Based on base population parameter estimates in 12-week-old male mice of a different line, Eisen and Prasetyo (1988) found that the lean index was expected to restrict fat content to approximately zero change. After seven generations of selection, fat weight was not different between the high and low lines, but the high lines had a higher body weight and protein weight (Sharp et al. 1984). However, asymmetry of response was found for body weight and fat weight; for body weight the response upward was much greater than the downward response, while for fat weight both lines were higher than controls. However, asymmetry of response in body weight may have been transient because it was not present in generations eight and nine. Therefore, the lean index was a reasonably successful restricted index.

Replicated restricted selection index experiments in *Tribolium castaneum* also revealed considerable disagreement between observed and theoretical responses (Scheinberg et al. 1967; Okada and Hardin 1967, 1970). Bohren (1975) suggested that replicate single generation selection experiments would be a more appropriate method of testing selection theory because the effects of genetic drift and inbreeding would be minimized. Garwood et al. (1978) reported good agreement between expected and observed responses in a replicated single generation restricted selection index study in poultry designed to increase egg weight and egg production without changing days tested. Campo and Villaneuva (1987) reported two replicated single generation restricted selection index experiments in *Tribolium castaneum* aimed at either increasing adult weight without changing pupal weight or increasing egg number without changing adult weight. Response in the unrestricted traits was less than expected, and the restricted traits responded positively. Therefore, the one generation selection approach, at least in this study, did not eliminate the problem of discrepancies between observed and predicted responses in restricted index selection studies.

Harris (1964) showed that progress from unrestricted index selection may be poorly predicted if estimation of genetic and phenotypic parameters are greatly different from the true population parameters, although the index seems to be robust in this regard. However, in the case of restricted index selection, poor estimation of parameters may cause the actual response in the restricted variable to differ markedly from that intended (Hill and Meyer 1984). Comparing several index selection experiments with *Tribolium*, Campo et al. (1990) found greater discrepancies between observed and expected responses when restricted and/or antagonistic indices were used. But it is difficult to see why poor parameter estimates would necessarily lead to asymmetry.

Eisen (1977) suggested that restricted index selection may be more sensitive to alterations in genetic parameters than single-trait selection. Mortimer and James (1987) examined the consequences of this hypothesis for two traits controlled by four loci. Most models they examined led to changes in gene frequency, which changed genetic parameters, causing an inability of the restricted index to maintain zero genetic change in the restricted trait. They pointed out that in a model with many loci each with small gene effects, this conclusion would still hold, although it might take longer for the effectiveness of the restricted index to be reduced. Asymmetry of responses was not discussed, but it is possible that asymmetry is as likely to occur in the component traits of the selection index as it was shown to be for correlated responses in single-trait selection (Bohren et al. 1966). Further, under the infinitesimal model, asymmetry in correlated responses to selection can be caused by linkage disequilibrium (Villaneuva and Kennedy 1992).

Other possible factors contributing to asymmetry of responses in component traits of the restricted index were the asymmetry in realized index weights and the smaller absolute cumulative selection differential applied to LE compared to HE. Both replicates of LE had a relatively higher than expected weighting factor applied to BW, which may have caused the positive response in BW. However, this factor is a questionable cause of asymmetry because the lower than expected weighting factor for BW in HE did not result in a reduction in BW. The relatively weak cumulative selection differential in LE may have caused genetic drift to lead to the positive response in BW just by chance. One possible way of increasing the selection differential would have been to have used mass selection rather than within-family selection. But then there would be the risk that effective population size would be greatly reduced, leading to a rapid increase in inbreeding.

Harvey (1972) developed the technique of estimating realized heritabilities and realized genetic correlations from two-trait selection index experiments. Applying this technique to the present selection study yielded results which are reasonable, considering the unexpected responses for BW and EF in the LE replicates. One can ask how reliable this technique is in general. Few studies have applied the technique, and those that have used the procedure have met with mixed success. Berger and Harvey (1975) applied the technique to a selection experiment for high-high, high-low, low-high and low-low 12- to 21-day gain and 51-day body weight in mice. Combined estimates of realized genetic parameters were consistent with offspring-sire estimates, but there was considerable variation among realized estimates. Rutledge et al. (1973) used the method to estimate realized genetic parameters in a selection index experiment in mice for high 6-week tail length-low 6-week body weight and vice versa. Realized heritabilities were in fair agreement with base population and single-trait realized estimates, but the realized genetic correlation was much higher than base estimates. The latter discrepancy may have been due to the antagonistic nature of the selection indices used. However, sampling effects, the nature of which are unknown, may also have been a factor. Eisen (1977) applied the technique to restricted selection index in mice aimed at increasing or decreasing 3- to 6-week postweaning gain while holding food intake constant. Realized heritability for postweaning gain was in agreement with a paternal half sib-estimate, but realized heritability for feed consumption was negative, which invalidated the realized genetic correlation. Eisen (1977) pointed out that multicollinearity among variables in the design matrix may have led to the negative realized heritability estimate. In summary, caution is needed in interpreting the method of estimating realized genetic parameters from two-trait index studies because little is known about its sampling properties and multicollinearity may lead to misleading estimates.

The present experiment confirmed earlier findings that realized responses in restricted index selection often do not agree with expectation. Asymmetry of responses in component traits of the index was observed, but responses in index units per se were not asymmetric. Possible explanations for these results include genetic drift, inaccurate estimates of genetic parameters, change in genetic parameters with selection, linkage disequilibrium and weak selection. The results indicate that application of restricted selection indices to livestock breeding will require careful monitoring of responses in each generation to determine if the intended changes are being realized.

Acknowledgements. The technical assistance of Ms. Beth Johnson and Ms. Linda Hester is acknowledged.

References

Abplanalp H, Ogasawara FX, Asmundson VS (1963) Influence of selection for body weight at different ages on growth of turkeys. Br Poul Sci 4:71–82

Becker WA (1984) Manual of quantitative genetics. Academic Enterprises, Pullman

Berger PJ, Harvey WR (1975) Realized genetic parameters from index selection in mice. J Anim Sci 40:38–47

Biswas DK, Hunt PV, Chapman AB, First NL, Self HL (1966) Feed efficiency and carcass desirability in swine. J Anim Sci 25:342–347

Bohren BB (1975) Designing artificial selection experiments for specific objectives. Genetics 80:205–220

Bohren BB, Hill WG, Robertson A (1966) Some observations on asymmetrical correlated responses to selection. Genet Res 7:44–57

Campo JL, Velasco T (1989) An experimental test of optimum desired-gains indexes in *Tribolium*. J Hered 80:48–52

Campo JL, Villaneuva B (1987) Experimental comparison of restricted selection index and restricted independent culling levels in *Tribolium castaneum*. Genome 29:91–96

Campo JL, de la Fuente B, Garciá Gil MC, Rodrígeuz MC, Velasco T (1990) Experimental results with linear selection indices in *Tribolium*. In: Hill WG, Thompson R, Woolliams JA (eds) Proc 4th World Cong Genet Appl Livest Prod, vol XIII, pp 345–348

Dickerson GE, Blunn ST, Chapman AB, Kottman RM, Krider JL, Warwick EJ, Whatley JA Jr, Baker ML, Lush JL, Winter LM (1954) Evaluation of selection in developing inbred lines of swine. Mo Agric Exp Stn Res Bull 551

Eisen EJ (1977) Restricted selection index: an approach to selecting for feed efficiency. J Anim Sci 44:958–972

Eisen EJ (1987) Selection for components related to body composition in mice: direct responses. Theor Appl Genet 74:793–801

Eisen EJ (1989) Selection experiments for body composition in mice and rats: a review. Livest Prod Sci 23:17–32

Eisen EJ (1992) Restricted index selection in mice designed to change body fat without changing body weight: correlated responses. Theor Appl Genet (in press)

Eisen EJ, Leatherwood JM (1978) Adipose cellularity and body composition in polygenic obese mice as influenced by preweaning nutrition. J Nutr 108:1652–1662

Eisen EJ, Prasetyo H (1988) Estimates of genetic parameters and predicted selection responses for growth, fat and lean traits in mice. J Anim Sci 66:1153–1165

Falconer DS (1989) Introduction to quantitative genetics, 3rd edn. Longman, Essex

Garwood VA, Lowe PC, Bohren BB (1978) A replicated single generation test of a restricted selection index in poultry. Theor Appl Genet 52:227–231

Harris DL (1964) Expected and predicted progress from index selection involving estimates of population parameters. Biometrics 20:46–72

Harvey WR (1972) Direct and indirect response in two-trait selection experiments in mice Proc 21st Nat Breed Roundtable. Kansas City

Hill WG (1972a) Estimation of realized heritabilities from selection experiments. I. Divergent selection. Biometrics 28:747–765

Hill WG (1972b) Estimation of realized heritabilities from selection experiments. II. Selection in one direction. Biometrics 28:767–780

Hill WG, Meyer K (1984) Effects of errors in parameter estimates on efficiency of restricted genetic selection indices. Hinkelmann K (ed) In: Experimental design, statistical models, and genetic statistics. Marcel Dekker, New York

Kempthorne O, Nordskog AW (1959) Restricted selection indices. Biometrics 15:10–19

Leenstra FR, Pit R (1988) Fat deposition in a broiler strain 3. Heritability of and genetic correlations among body weight, abdominal fat, and feed conversion. Poul Sci 67:1–9

Lin CY, Allaire FR (1977) Heritability of a linear combination of traits. Theor Appl Genet 51:1–3

McCarthy JC, Doolittle DP (1977) Effects of selection for independent changes in two highly correlated body weight traits in mice. Genet Res 29:133–145

Mortimer SI, James JW (1987) Changes in genetic parameters under restricted index selection. Genet Res 49:129–134

Nordksog AW (1978) Some statistical properties of an index of multiple traits. Theor Appl Genet 52:91–94

Nordksog AW, Tolman HS, Casey DW, Lin CY (1974) Selection in small populations of chickens. Poul Sci 53:1188–1219

Okada I, Hardin RT (1967) An experimental examination of restricted selection index, using *Tribolium castaneum*: 1. The results of two-way selection. Genetics 52:227–236

Okada I, Hardin RT (1970) An experimental examination of restricted selection index, using *Tribolium castaneum:* II. The results of long-term one-way selection. Genetics 64:533–539

Rutledge JJ, Eisen EJ, Legates JE (1973) An experimental evaluation of genetic correlation. Genetics 75:709–726

Scheinberg E, Bell AE, Anderson VL (1967) Genetic gain in populations of *Tribolium castaneum* under unistage tandem selection and under restricted selection indices. Genetics 55:69–90

Sharp GL, Hill WG, Robertson A (1984) Effects of selection on growth, body composition and food intake in mice. I. Responses in selected traits. Genet Res 43:75–92

Stewart TS, Schinckel AP (1990) Genetic parameters for swine growth and carcass traits. In: Young LD (ed) Genetics of swine. USDA, ARS, Clay Center, pp 77–79

Villaneuva B, Kennedy BW (1992) Asymmetrical correlated responses to selection under an infinitesimal genetic model. Theor Appl Genet (in press)

Young SSY (1961) A further examination of the relative efficiency of three methods of selection for genetic gains under less restricted conditions. Genet Res 2:106–121