

GENETIC CORRELATION BETWEEN GROWTH RATE AND LITTER SIZE IN MICE¹

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QUANTITATIVE geneticists have long been aware that correlated responses are common in populations under different types of selection. The primary implication of a correlated response is that the character under selection is genetically correlated with another character, though other parameters affect the magnitude of the correlated response.

In the course of selection for a single trait, other than a trait pertaining to reproduction, for an extended period of time, one expects sooner or later to encounter a decline in fertility or net reproduction. This has been reported by WIGAN and MATHER (1942), MATHER and HARRISON (1949), ROBERTSON and REEVE (1952), CLAYTON, MORRIS and ROBERTSON (1957) and LERNER (1958).

The purpose of this paper is to report on the correlated response of litter size to recurrent selection for post-weaning growth in an experimental population of mice. MACARTHUR (1949) and FALCONER (1955) have both reported increases in litter size associated with selection for large body size and decreases in litter size associated with selection for small size in mice.

EXPERIMENTAL PROCEDURE

The data summarized in this manuscript were obtained during the first 30 generations of a selection experiment initiated in 1957 and reflect selection practiced during 29 successive generations. They were obtained on offspring of 20 or more sires each generation. Number of litters per sire varied from one to three and averaged more than two. Technical details not given below were described in earlier papers by RAHNEFELD, BOYLAN and COMSTOCK (1962) and RAHNEFELD, BOYLAN, COMSTOCK and SINGH (1963).

Three populations (lines), S, S¹ and A, provide the data for this report. The S-line is a segregating population formed from the reciprocal crosses of two unrelated inbred lines. The F₂ was designated generation zero of the S-line. Selection in the S-line has been for one trait, post-weaning growth (measured to the nearest 0.1g) from weaning to 42 days of age. Mice were weaned at 21 days in generation 1 and at 18 days thereafter. Selection was initiated among generation 1 animals and has been applied in all succeeding generations. Generations have been nonoverlapping. Individual breeding animals have been used to produce offspring in only one generation. Inbreeding has been slow because offspring from 20 or more sires were reared in each generation. Matings among selected individuals have been random except that full-sib matings were avoided.

The S¹-line was formed from the same inbred lines as the S-line and by exactly the same

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procedure but 15 generations later. Because the foundation lines were highly inbred, the two lines must have been nearly identical in genetic constitution at generation zero. The S¹-line has been managed the same in all respects as the S-line, including procedure in selection. The purpose was to obtain, by comparison of the two lines, another measure of response to selection in the S-line. Since the S¹-line was initiated 15 generations after the S-line, S¹₁ was contemporary with S₁₆, S¹₂ with S₁₇,, and S¹₅ with S₂₀.

The A-line is a derivative of a standard laboratory inbred (Balb/c). It traces completely to one pair of full sibs produced by over 60 generations of continuous full-sib mating. During the course of the experiment the A-line has been maintained as a closed population with random mating among breeding animals chosen at random. Minimum genetic change during the course of the experiment was anticipated in the case of this line because (a) it was highly inbred at the outset and (b) the only deviations from random selection were those arising from natural causes. RAHNEFELD *et al.* (1963) reported, using data from 18 generations, estimates of additive genetic variance for post-weaning growth in the A-line of 0.037 ± 0.087 and -0.012 ± 0.042 for males and females respectively. In view of standard errors shown, these do not establish complete absence of additive genetic variance. On the other hand, they provide no positive evidence for genetic variation in the line.

Performance averages for the A-line were employed as control measures of variation in environment. It is worth noting in this connection that there was significant intercycle variation in the averages of both growth and litter size but that neither trait exhibited a long-time, trend in this line.

In all three lines, each litter was raised in a single container to 42 days of age. Weaning was accomplished by removal of the dam.

Data recorded have been sex, 18- and 42-day weights, litter size at weaning and at 42 days, and feed consumption (total feed) by litters in the post-weaning (18-42 day) period.

STATISTICAL PROCEDURE

Estimation of the genetic correlation between litter size and post-weaning growth required estimates of additive genetic variance in each of these variables and of the additive genetic covariance between them. Procedures in obtaining these estimates were largely as described by RAHNEFELD *et al.* (1962) and RAHNEFELD *et al.* (1963).

The estimate of additive genetic covariance was based on covariance between post-weaning growth of dam and litter size of daughter as outlined in 1962. The estimate of additive genetic variance in post-weaning growth was based on analyses of variance and parent-offspring regressions using procedures detailed in 1963. Additive genetic variance in litter size was estimated from dam-offspring covariance, as described in 1962, and from intra-cycle analyses of variance. In obtaining the approximations to $V(S)$ that were employed in getting the weighted average of estimates of the sire effect variance (S) from separate intra-cycle variance analyses: (1) a single value for D (the variance of dam effects), obtained by ordinary pooling of the separate variance analyses, was employed in the numerical approximations to the mean square expectations, and (2) the single value employed for S in these same approximations was one quarter of the additive genetic variance estimate obtained from dam-daughter covariance. There was no reason to believe D variable from cycle to cycle as there was in the case of post-weaning growth; hence the decision to employ a common value. The dam-daughter covariance source for the approximation to S was chosen because the pooled variance analyses estimate was negative and therefore not acceptable.

Averages of estimates were frequently computed. In all cases, weighted averages were employed, the weights used being inversely proportional to the estimated variances of quantities averaged.

RESULTS AND DISCUSSION

The additive genetic covariance between post-weaning growth and litter size

in the S-line was estimated as 0.200 ± 0.222 (1682 df associated with the estimate) after correction for bias due to selection of parents. When parent-offspring covariance is estimated from data involving parents that have been selected on the basis of the parent measurement involved in the covariance, the result is biased downward relative to the total population covariance. This was the situation since parents had been selected for growth. Bias was removed by multiplying the raw estimate by the ratio of total phenotypic variance among unselected individuals to the total phenotypic variance among selected parents contributing to data employed for computing covariance. The estimates of phenotypic variance in gain among dams and among all females used in adjusting the dam-offspring estimate of additive genetic covariance, were 0.55 and 1.84 respectively.

Estimates of variance components and additive genetic variance for litter size representing information from all data of the 30 cycles in the S-line are listed in Table 1 and Table 2.

The heritability estimate for litter size, computed using the average value from Table 2 and the estimate of total phenotypic variance (P) from Table 1, is 0.040 ± 0.037 . FALCONER (1960) reported that the heritability of litter size in

TABLE 1

Estimates of variance components for litter size (S-line)

Component	Symbol	df	Estimate
Sire	<i>S</i>	520	-0.083 ± 0.121
Dam (litter)	<i>D</i>	333	0.532 ± 0.165
Within litter	<i>W</i>	829	3.106 ± 0.141
Total	<i>P</i>	1682	3.555

TABLE 2

Estimates of additive genetic variance for litter size (S-line)

Source of estimate	Additive genetic variance
Components of variance	-0.330 ± 0.484 (520 df for sires)
Dam-offspring covariance	0.18 ± 0.135 (1682 df)
Average	0.143 ± 0.131

TABLE 3

Estimates of variance components for female growth rate (S-line)

Component	Symbol	df	Estimate
Sire	<i>S</i>	663	0.083 ± 0.030
Dam (litter)	<i>D</i>	808	0.624 ± 0.049
Within litter	<i>W</i>	3894	1.131 ± 0.026
Total	<i>P</i>	5365	1.838

TABLE 4

Estimates of additive genetic variance for female growth rate (S-line)

Source of estimate	Additive genetic variance
Components of variance	0.332 ± 0.119 (663 df for sires)
Dam-offspring covariance	0.367* ± 0.123 (1459 df)
Average	0.349 ± 0.086

* Corrected for bias due to selection of parents.

mice was approximately 0.15. DALTON and BYWATER (1963) estimated heritability of litter size at weaning to be 0.06.

The variance component estimates for female growth rate in the S-line are listed in Table 3. Estimates of additive genetic variance for female growth rate representing information from all data in the S-line are listed in Table 4.

The heritability estimate for female growth rate using the average value from Table 4 and the estimate of P from Table 3, is 0.190 ± 0.047 . FALCONER (1960) reported 0.175 as an estimate of realized heritability from intra-litter selection. Given no concurrent natural selection or no genetic correlations of growth with components of fitness this realized heritability estimates $G/2W$ where G and W are additive genetic variance and intra-litter phenotypic variance, respectively. For comparison our estimates of G and W yield the following estimate of intra-litter heritability, $(.349)/2(1.131) = 0.154$.

Finally, the genetic correlation between post-weaning growth and litter size is estimated to be $0.200/\sqrt{(0.143)(0.349)} = 0.89$.

If the genetic correlation is in fact large, the selection exerted for gain in the S-line should have resulted in considerable increase in litter size as a correlated response. The magnitude of this response can be estimated (1) by regression of the difference between the S- and A-lines on generation time and (2) by the difference between the S- and S¹ lines. The S- and A-line averages for litter size by generations are listed in Table 5.

The estimate of linear regression of the S-line and A-line difference on generation time was 0.099 ± 0.011 . Statistical test showed no significant deviation from linear regression. Multiplication by 29 yields 2.87 ± 0.319 as the estimate of correlated response in litter size to selection for growth in the period from generation 1 to generation 30 in the S-line. In Table 6 are listed the averages for contemporary generations in the S- and S¹-lines. The mean difference was 1.64. It must be divided by 15, the generation time lag between S and S¹, to provide an estimate of change per generation. The result is 0.109, which is almost identical with the regression estimate. Multiplying this by 29 the estimate is 3.16 as the total correlated response in litter size. This positive response to selection for post-weaning growth is qualitatively comparable to the responses in litter size that MACARTHUR (1949) and FALCONER (1955) observed in populations selected for large body size. However, in their experiments the correlated response ceased

TABLE 5

*Average litter size by generations**

Cycle	S population	A line	Difference
1	6.90	6.39	.51
2	7.23	5.41	1.82
3	6.16	4.23	1.93
4	6.00	4.45	1.55
5	6.77	6.10	.67
6	6.71	5.16	1.55
7	6.04	4.96	1.08
8	5.25	3.77	1.48
9	6.20	4.44	1.76
10	7.97	5.42	2.55
11	6.88	5.03	1.85
12	5.88	3.93	1.95
13	7.07	4.97	2.10
14	8.31	5.15	3.16
15	7.06	4.88	2.18
16	7.35	4.89	2.46
17	7.98	5.37	2.61
18	8.82	5.73	3.09
19	7.55	4.45	3.10
20	6.92	4.04	2.88
21	8.80	5.10	3.70
22	9.75	5.46	4.29
23	8.49	4.77	3.72
24	7.02	3.61	3.41
25	9.38	5.39	3.99
26	8.73	5.43	3.30
27	7.82	4.56	3.26
28	7.98	4.10	3.88
29	9.10	5.30	3.80
30	9.27	6.68	2.59

* Litter size measured as the number of mice weaned.

after a very few generations (five in one case and six in the other) while in ours there has been no clear indication of change in response during the 29 generations of selection for which results are reported. This difference is probably a function of the difference in selection criterion. For dams of equal size there would be a negative correlation between litter size and weight of offspring at 42 or 60 days and a resultant tendency for mice largest in size to be found in smaller litters. The litter size effect on post-weaning growth is much less than on weight at 42 days and not sufficient to dampen the correlated response.

Both expected and effective selection differentials, as defined by FALCONER (1960), were computed each generation. Weighting of the parents record in the case of the effective selection differential was by number of offspring that lived to 42 days of age. The ratio of effective to expected differentials was computed for each generation. Its average value was 1.000, its standard deviation was 0.022,

TABLE 6

Average litter size in contemporary generations of the S and S¹ populations

Cycle in S population	S population	S ¹ population	Difference
16	7.35	5.74	1.61
17	7.98	6.40	1.58
18	8.82	7.44	1.38
19	7.55	5.81	1.74
20	6.92	5.05	1.87
Average	7.72	6.09	1.64

and there was no time trend in its magnitude. These observations indicate no correlation, among selected parents between growth rate and number of offspring left in the population.

The next question is whether the observed response agrees with the predicted response based on quantitative genetic theory and the appropriate parameter estimates. The theoretical response is $T Cg/P$, where T is the selection differential for gain totalled for the 29 generations of selection, P is population phenotypic variance in gain and Cg is the additive genetic covariance between gain and litter size. The estimate of T is 71.41 g for males and 37.42 g for females, and of P is 3.11 for males and 1.83 for females. Using simple averages and the estimate of Cg (0.200) the predicted response in litter size is $(54.41) (.200)/(2.47) = 4.49$. Thus the estimate of actual response is $(2.87)/(4.49) = .64$ of the predicted.

The difference between observed and predicted response in litter size may have resulted entirely from overestimation of the additive genetic covariance between growth rate and litter size; the standard error (.22) of the estimate does not exclude the possibility that the actual covariance was considerably smaller than the 0.20 estimate obtained. On the other hand there may be strong dependence of litter size on body size and, if so, the difference between observed and predicted response may reflect the similar difference in the case of post-weaning gain itself. The ratio of observed to predicted response for gain was also 0.64. As noted by RAHNEFELD *et al.* (1963), that difference may have reflected a biological reality but was in fact not significant.

There are good reasons to anticipate that continued selection for an extreme in a trait like growth rate will result eventually in reduced reproduction (fitness); see LERNER (1958) in particular. However, it is not clear *a priori* that loss of fitness must always occur as a correlated response to selection for a metric trait or how soon reduction in fitness should be expected. Against this background the fact that litter size has increased through most, if not all, of the 30 generations of selection for growth rate is significant and exceedingly interesting. This observation is in strong contrast to the decrease in hatchability within five generations of selection for shank length in White Leghorns reported by LERNER (1958).

SUMMARY

The genetic correlation and additive genetic covariance of post-weaning gain and litter size were estimated for a genetically variable population of mice during a 29-generation span in which recurrent selection for post-weaning gain was practiced. Estimates indicate a high positive genetic correlation (0.89).—The total response in litter size to direct selection for gain was 0.099 per generation or a total of 2.87 for 29 generations. This was 64% of the response predicted using the standard prediction formula. There was no statistically significant deviation from linearity in the regression of mean litter size on generation time.

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