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Effect of Selection for Spot Size on Reproduction and Body Weight in Mice*

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Summary. Spot size in descendants from the Goodale white-spotted stock of mice responded to selection for increased spot size. The realized heritability estimate was 0.52. However, no correlated response of reproduction to spot size selection was found in the present study, nor was there any correlated response among body weight variables.

Key words: Selection – Correlated response – Reproduction – Body weight – Spot size

Introduction

Doolittle (1979) showed that the presence of spots in the Goodale white-spotted mouse stock (Doolittle et al. 1975) was due to a single autosomal gene while the size of spots was a quantitative character responding to selection. He also found that litter size at birth and weaning ratio (proportion of mice born surviving to weaning age) declined as spot size increased under selection, and returned to normal levels when spot size selection was reversed in the selected lines. The present study was undertaken to provide further information on correlated responses of body weight and reproductive traits to selection for spot size.

Materials and Methods

At the conclusion of the study reported by Doolittle (1979) the two selected lines, which had been rendered homozygous for the major gene causing head spots, were crossed. F_1 offspring of the cross were randomly mated without selection to produce an F_2 generation. From among these F_2 offspring 60 mice of each sex were chosen at random, and randomly paired. Thirty pairs were mated immediately, the other thirty pairs two weeks later, to form the unselected control lines for two replicates. From the remaining F_2 offspring 60 mice of each sex with the largest spots were chosen and randomly paired. Thirty pairs were mated immediately, thirty pairs two weeks later, to form the selected lines for the two replicates.

In each subsequent generation, 30 mice of each sex were randomly chosen from each control line, and randomly mated by pairs. From each selected line, the 30 mice of each sex with largest spots were chosen and randomly mated by pairs. The experiment was continued over four generations of selection.

Schiable (1969) described fourteen pigmentation areas in the mouse. Spot size in the present study was scored by counting the number of these areas in which white hairs appeared at weaning age (21 ± 1 days). In addition to counting numbers of mice born and weaned per litter, mice were individually weighed at 21 and 42 days of age. Only first litter results were used. Spot score, fertility ratio (proportion of mated pairs producing a litter), litter size at birth, weaning ratio, body weights at 21 and 42 days old, and body weight gain between these two ages (post-weaning gain) were analyzed. For each variable, subgroups were defined by replicate, line and generation, and for the weights, weight gains and spot scores, also by sex. Subgroup means were calculated and subjected to analyses of variance. Error terms were derived from within subgroup variances except for the fertility ratio, where multiple factor interactions were used. Fertility and weaning ratios were transformed using the arc sine of the square root of the ratio, and spot scores using the logarithmic transformation.

Results

Spot score averages are shown in Table 1. Analyses of variance showed the following differences to be significant. Male mice had spots 0.2 units larger than females. Replicate 2 mice had spots 0.5 units larger than replicate 1 mice. Spots in the selected lines were 1.9 units larger than in the unselected lines. The linear regression of spot size on generation number was +0.9 units per generation in the selected lines, while in unselected lines it was +0.1 units per generation. Realized heritability estimates, from the regres-

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Table 1. Subgroup averages for spot size (units)

		Replicate 1		Replicate 2	
		♂	♀	♂	♀
Base		2.95	2.54		
Unselected	1	2.34	2.27	2.49	2.29
	2	2.74	2.30	2.82	2.51
	3	2.43	2.64	3.17	3.09
	4	2.89	2.78	3.36	3.49
Selected	1	2.93	2.70	3.62	3.10
	2	3.53	3.69	4.48	4.17
	3	5.17	4.95	5.58	5.10
	4	5.87	5.79	6.84	6.50

Table 2. Subgroup averages for reproduction variables

		Replicate 1			Replicate 2		
		FRA[a]	LSB[b]	WRA[c]	FRA	LSB	WRA
Base		0.90	9.09	0.92			
Unselected	1	0.90	9.74	0.93	0.97	9.21	0.90
	2	0.80	8.58	0.74	0.73	7.50	0.82
	3	0.87	8.92	0.82	0.93	7.93	0.85
	4	0.90	8.22	0.91	0.80	7.67	0.96
Selected	1	0.87	9.54	0.89	0.80	9.42	0.95
	2	0.90	9.22	0.91	0.90	8.63	0.87
	3	0.87	8.31	0.89	0.93	8.43	0.88
	4	0.83	8.12	0.95	0.80	7.21	0.95

[a] FRA = no. of first litters born/no. of matings = fertility rate

[b] LSB = no. of pups born/no. of litters born = litter size at birth

[c] WRA = no. of mice weaned/no. of pups born = weaning rate

Table 3. Subgroup averages for body weight variables (grams)

	Unselected				Selected			
	Replicate 1		Replicate 2		Replicate 1		Replicate 2	
	♂	♀	♂	♀	♂	♀	♂	♀
21 day weights								
Base	9.91	9.61						
1	10.24	9.26	10.19	10.10	10.00	10.27	9.86	9.48
2	9.73	9.82	10.52	9.85	10.11	9.59	10.35	9.36
3	8.86	8.73	9.02	8.88	8.88	9.39	8.74	8.56
4	10.06	9.76	11.30	10.35	11.02	10.01	9.48	9.31
42 day weights								
Base	24.13	20.17						
1	22.95	19.33	23.64	19.72	22.95	19.74	23.10	19.77
2	22.73	19.91	23.86	19.57	23.19	19.32	23.16	19.07
3	21.23	18.00	20.89	17.86	20.62	17.86	20.12	17.00
4	22.22	18.90	25.20	19.89	23.63	19.09	22.06	18.63
Post-weaning gains								
Base	14.22	10.56						
1	12.71	10.07	13.17	10.10	12.95	10.27	13.24	10.29
2	13.00	10.09	13.33	9.72	13.08	9.73	12.81	9.20
3	12.37	9.27	11.87	8.98	11.74	9.39	11.37	8.44
4	12.16	9.14	13.90	9.54	12.61	9.08	12.59	9.31

sion of cumulative response on cumulative selection differential, were 0.53 ± 0.06 and 0.50 ± 0.05 in replicates 1 and 2, respectively. These estimates are similar to those obtained by Doolittle (1979).

Subclass averages for fertility ratio, litter size at birth, and weaning ratio are presented in Table 2. Fertility varied considerably from subclass to subclass, but no significant trends associated with replicate, selection or generation appeared. Litter size at birth differed significantly between replicates, replicate 1 producing 0.6 pups/litter more than replicate 2 matings. There was also a significant linear decline in litter size with generations, the regression being 0.5 pups/litter/generation. However, neither litter size nor the regression of litter size on generations differed between selected and unselected lines.

There was a significant effect of generations on weaning ratio, but this was quadratic; weaning ratios in generations 2 and 3 were about 7.5% less than in generations 1 and 4. Selected and unselected lines differed significantly in weaning ratio; the selected lines weaned 4% more of their pups than the unselected lines. The relationship between weaning ratio and generation number was similar in selected and unselected lines.

Subgroup averages for the body weight variables are presented in Table 3. Males weighed 0.4g more than females at 21 days of age. Males weighed 3.6g more than females at 42 days old. Weights at 42 days of age decreased with generation number, the linear regressions being –0.4g/generation, but these regressions were similar in all four lines. Males gained 3.2g more than females in the post-weaning period. Although replicates on the average did not differ in post-weaning gain, and selected and unselected lines were equal in post-weaning gain in replicate 1, in replicate 2 unselected lines gained 0.2g more than in replicate 1, while selected lines gained 0.2g less in the later replicate. Therefore, unselected lines gained 0.2g more than selected lines over all. As with 42 day weight, there was a –0.4g/generation linear regression of post-weaning gain on generation number, this regression being similar in all four lines.

There was therefore no evidence of a correlated response of either reproductive or body weight traits to selection for spot size. The only reproductive trait showing a significant difference between selected and unselected lines was weaning ratio, where selected lines were actually superior to unselected. The only body weight trait showing such a difference was post-weaning gain, with unselected lines being superior. In none of the variables was there a difference in regression on generation number that a correlated response to spot size selection should have created.

Discussion

The evidence of this and of the previous study (Doolittle 1979) shows clearly that spot size is a quantitative trait which responds to selection. The heritability is relatively high, near 0.5. This trait may provide an alternative to body weight and reproductive traits for quantitative genetic studies in the mouse.

The significant correlated response of reproductive traits to spot size selection reported by Doolittle (1979) was, however, not found in the present study. The earlier correlated response could have been caused by spot size genes with significant pleiotropic effects on reproduction, and the disappearance of the effect in the present study by fixation of loci affecting both spot size and reproduction. However, fixation of those loci would be expected to decrease the heritability of spot size. Since there was no such decrease, it seems unlikely that any significant number of loci existed with effects on both spot size and reproduction gains.

Unless the association of these traits in the earlier study was purely spurious, the most reasonable explanation would seem to be linkage between loci affecting spot size and reproduction. The original study was performed on mice descended from a cross between the Goodale white-spotted stock (Doolittle et al. 1975) and Hauschka's Breeder HA (ICR) stock (Hauschka and Mirand 1973). Linkage between genes for large spot size and genes for poor reproductive performance gains some credence from the nature of these stocks. The Goodale stock, presumably the source of most of the large spot genes in the cross progeny, reproduced poorly, while the Hauschka stock had been selected for large litters and high weaning ratios.

Although four generations of random mating had been allowed to elapse after the stocks were crossed before selection began, linkage disequilibrium may still have existed when the earlier selection study was initiated. The disequilibrium had evidently been dissipated before the study reported in this paper began.

Litter size decreased sharply over the four generations in this study in all four lines. Body weights also decreased, though more moderately. It is not clear what caused these decreases. The lines were maintained using 30 matings per generation in each line. This permitted a certain amount of inbreeding, even in the unselected controls, but the rate of inbreeding was low. In numerous other studies in this laboratory (e.g. Doolittle 1979), lines have been maintained using 30 matings per generation without undue deleterious effect on litter size or body weight. Furthermore, the four lines were kept separate for an additional generation beyond the end of this study, using 30 matings per line. In that generation, litter size rebounded sharply, to an average of 8.7 mice per litter. Inbreeding (or random genetic drift) due to the restricted number of matings appeared to be unlikely as a cause for these decreases.

Generation 1 litters were born in the early summer of 1979. Subsequent generations followed at approximately three month intervals thereafter, generation 4 litters being born in early spring, 1980. Despite control of the environment in the mouse rooms, mouse stocks have shown some seasonal variation in reproductive performance, the best performance occurring in late spring or early summer. The magnitude of this variation has been too slight to account for the decreases noted in the present case. However, an abnormally strong seasonal trend, enhanced by inbreeding and possibly by other unknown factors, appeared the best explanation for the decreases in litter size and body weight observed in this study.

Since these decreases affected both control and selected lines equally, they did not invalidate the comparison between these lines which was the object of the study.

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