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Heterosis among lines of mice selected for body weight

2. Reproduction

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Summary. To examine the effect of selection for body weight on levels of heterosis for reproductive traits, crosses were made between three groups of six lines of mice, one group unselected (controls) and the other two selected for high (large lines) and low (small lines) 6-week body weight, respectively. The coefficient of inbreeding of each line was about 0.60. In a comparison of purebred and crossbred progeny, both out of purebred mothers, there was on average 4% heterosis for number born, 3% for percentage weaned and 8% for numbers weaned. In a comparison of purebred and crossbred mothers, each mated to males of an unrelated strain and dissected on the 17th day of gestation, crossbreds had on average 1.6 more live embryos, which was 22% of the purebred mean. This comprised an increase of 0.6 corpora lutea, of 0.4 in survival to implantation and of 0.6 in subsequent survival to 17 days. The heterosis was similar whether the mothers had parents of the same or different size.

Key words: Heterosis – Reproduction – Mice – Body weight

Introduction

In a previous paper (Bhuvanakumar et al. 1985) we reported on the extent of heterosis for growth-related traits among replicated lines of mice selected for high or low 6-week body weight, together with controls (Falconer 1973). Heterosis was observed for 6-week weight and gain from 3–6 weeks, but not for 3-week weight. There was no more heterosis between crosses of lines of different size than between lines of the same size, but there was more heterosis among crosses of large selected lines than among those of small selected lines.

It is a common observation that reproductive traits such as ovulation rate, embryonic and post-natal survival and litter size show more heterosis than traits of growth. For example, results for a range of species are listed by Falconer (1981), extensive data for pigs are given by Sellier (1976) and for mice by Roberts (1965). In this paper we investigate the extent of heterosis for reproduction in mice and how it relates to the body size of the parents, both for purebred females mated either pure or cross, and for purebred and crossbred females mated to an unrelated strain.

Materials and methods

The lines used for this study were the Q strains selected by Falconer (1973) for large (L) or small (S) body weight at six weeks, together with unselected controls (C), there being six replicates of each (labelled A–F). The design of the crossing experiment is given by Bhuvanakumar et al. (1985). Essentially crosses were made in three non-contemporaneous blocks: in block 1 the A lines were mated pure and with the large, control and small B line, similarly the B lines were mated pure and with large, control and small A. In block 2 the C and D lines and in block 3 the E and F lines were mated in the same fashion. The crosses were repeated over five phases, using mice from generation 59 and 61–64 of the Q lines, when the inbreeding coefficient of each line was approximately 0.60.

The first set of data reported here is on the litter size at birth (alive plus dead) and litter size of survivors at weaning of these purebred mothers mated either pure or cross. These data

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were analysed by least squares analysis of variance (Harvey 1977), fitting effects for: overall mean, phase, heterosis (pure or cross mating), size of female (L, C or S), block (AB, CD or EF lines), block × size of female interaction (which includes effects of drift among replicate lines since each block comprises a different set of lines), and error. No effects of size of mate were included since a preliminary analysis showed these effects were negligible (Bhuvanakumar 1980).

The second set of data is on components of reproduction of pure and crossbred mothers having crossbred offspring. In two phases the purebred and crossbred females from the first set of matings were all pair mated to males of the unrelated strain C57BL/Fa. The females were checked daily for copulatory plugs and were dissected on the 17th day of gestation. The following were recorded: a) the number of corpora lutea, as a measure of the number ovulated, b) the number of live embryos, and c) the number of resorptions and moles, as a measure of post-implantation loss. From these, pre-implantation loss was obtained as a-b-c, and total embryonic loss as a-b. In one phase a small number of mice were not dissected prior to parturition, and litter size at birth was recorded to check the extent of perinatal loss. The least squares analysis followed that used by Bhuvanakumar et al. (1985) for growth traits, except that effects for sex were not fitted. The model included: overall mean, phase, heterosis (purebred or crossbred female), size of sire of the female, size of dam of the female, size of sire × size of dam (estimated only among crossbred females), block, block × heterosis, block × sire size, block × dam size and residual error (which combined between and within litter of birth of the dam, since the former effects were trivial). Tests for main effects (e.g. heterosis) were made against the appropriate interaction with blocks (e.g. heterosis × blocks) because these interactions include drift error due to the nesting of lines within blocks.

Results

Litter size in purebred versus crossbred matings

Numbers of animals and least squares means for litter size at birth and weaning and for percentage weaned are given in Table 1. The average heterosis was 0.3 mice or 4% (as a percentage of the purebred mean) for numbers born, 0.6 or 8% for numbers weaned, and 3% for percentage weaned; it was highly significant for the latter two traits (Table 2). The interaction between size of dam and heterosis was non-significant, although the biggest purebred litters were from control mothers and the biggest crossbred litters were from large mothers. Averaged over purebreds and crossbreds, the litter size at birth of the large females exceeded that of the controls by 0.56 which in turn exceeded those of the small females by 1.62. The large lines had the lowest percentage weaned, however.

Table 1. Litter size from purebred mothers with either purebred or crossbred offspring: numbers of litters and least squares means

Size	Female 6-wk wt[a] (g)	Litters		No. born		No. weaned		% weaned	
		Pure	Cross	Pure	Cross	Pure	Cross	Pure	Cross
Large	26.5	92	210	9.50	9.95	7.67	8.77	83.1	86.8
Control	19.1	103	296	9.08	9.25	7.78	8.19	88.4	89.3
Small	13.9	84	255	7.39	7.69	6.49	6.74	89.6	88.8
Total/mean		279	761	8.65	8.97	7.31	7.90	86.1	89.2
Heterosis ± SE[b]				0.31 ± 0.18		0.59 ± 0.18		3.2 ± 1.1	

[a] Different data set (Bhuvanakumar et al. 1985)
[b] Approximate SE computed from within-cell variance

Table 2. Litter size from purebred mothers with either purebred or crossbred offspring: extract from analysis variance[a]

Source	df	Mean squares			Test vs[b]
		No. born	No. weaned	% weaned	
Heterosis (Het)	1	19.06	68.68**	1,966**	Het × Bl
Het × Dam Size (DS)	2	1.32	12.50	511	Het × DS × Bl
Het × Block (Bl)	2	9.99	5.39	7	Remainder
Het × DS × Bl	4	7.12	10.14	172	Remainder
Remainder	1,018	6.559	6.151	277.7	

[a] Source, df and mean squares not shown for effects of secondary interest (total df = 12)
[b] Error line used unless smaller than Remainder, when Remainder was used
* $P < 0.05$; ** $P < 0.01$

Components of litter size from purebred versus crossbred mothers

Numbers of litters and least squares means according to genotype of the female are shown in Table 3. Values of heterosis are given Table 4, computed as by Bhuvanakumar et al. (1985).

Table 3. Components of litter size from purebred and crossbred mothers mated to an unrelated strain: number of litters and least squares means

		No. of litters				
		Crossbred				Purebred
Sire	Dam	L	C	S	Total	
L		22	21	31	74	16
C		21	26	22	69	38
S		29	21	29	79	38
Total		72	68	82	222	92
		Least squares means				
		Crossbred				Purebred
Sire	Dam	L	C	S	Mean	
		Corpora lutea				
L		16.36	15.53	12.80	14.90	16.06
C		15.31	13.04	11.00	13.12	11.80
S		12.43	11.59	9.44	11.15	9.52
Mean		14.70	13.39	11.08	13.06	12.46
		Preimplantation loss (by difference)				
L		5.14	4.74	2.85	4.24	6.15
C		4.63	2.14	1.93	2.90	1.96
S		1.88	2.40	1.15	1.81	2.13
Mean		3.88	3.09	1.98	2.98	3.41
		Postimplantation loss				
L		1.18	1.47	0.38	1.01	2.04
C		1.05	0.28	1.67	1.00	1.50
S		0.87	0.68	0.90	0.82	1.14
Mean		1.03	0.81	0.98	0.94	1.56
		Live embryos				
L		10.04	9.31	9.57	9.64	7.87
C		9.63	10.62	7.40	9.22	8.35
S		9.69	8.51	7.39	8.53	6.26
Mean		9.79	9.48	8.12	9.13	7.49
		Embryonic survival %				
L		64.2	61.3	76.2	67.2	50.9
C		64.5	83.7	68.4	72.2	70.7
S		76.3	74.7	79.4	76.8	64.6
Mean		68.3	73.2	74.7	72.1	62.1

Overall, there is an increase of about 0.60 or 5% for crossbreds over purebreds in ovulation rate (number of copora lutea). The embryonic survival is higher in litters born to crossbred mothers, such that the differences in the number of live embryos is about 1.7 or 22% above the purebred mean. There is little clear indication of differential heterosis between large or small body size groups for any trait, nor between the same and different size crosses (Table 4), but the controls appear to show more heterosis for number of corpora lutea and compensating negative heterosis for preimplantation loss.

In the small trial in which litters were taken to term, the mean litter size at birth of 40 crossbred mice, roughly balanced over the 9 crosses, was 9.94 and that of 15 purebred mice was 8.53, a difference of 1.41. This value of heterosis in numbers born is very similar to the value of 1.6 for live 17-day embryos in the more extensive trial (Table 3).

Extracts from the analyses of variance of the components of litter size are given in Table 5. Although there was substantial heterosis in absolute terms, the low power of the test for heterosis, against block × heterosis with only 2 d.f., resulted in none of the tests for heterosis being significant.

Discussion

In the previous paper (Bhuvanakumar et al. 1985) we reviewed the deficiencies of the experimental design, in particular that each line was mated to only one other of each size. The problems of testing for heterosis effects against the 2 d.f. for heterosis × block interaction shown in Tables 2 and 5 illustrate these further.

After selection ceased almost 40 generations before the present crossing experiments commenced, reproductive performance in the small body weight lines improved. This is illustrated by the following approximate values, taken from Falconer (1973) and averaged over the last three generations (21–23) of selection, which can be compared with Table 1.

	L	C	S
No. born alive (from fertile matings)	9.2	9.0	6.4
Percentage weaned (of live births)	87	89	92

There were also many unproductive matings (24%, 12% and 27% in L, C and S, respectively) when selection ceased. The initial loss of performance can not be due solely to reduced homozygosity, for the lines were twice as inbred, 60% vs 30%, approximately, by the time the crosses were made. Obviously, the correlated changes induced by artificial selection had not been

Table 4. Components of litter size from purebred and crossbred mothers mated to an unrelated strain: heterosis estimates averaged over reciprocal crosses, by size of parent, by whether the cross was between or within size of parent, and overall (Mu)

	L	C	S	Mean	Between	Within	Mu (SE)[a]
	Corpora lutea						
L	0.30	1.49	−0.17	0.54	0.65	0.49	0.60(0.29)
C		1.24	0.63	1.12			
S			−0.08	0.13			
	Preimplantation loss (by difference)						
L	−1.01	0.63	−1.77	−0.72	−0.34	−0.61	−0.43 (0.38)
C		0.18	0.12	0.31			
S			−0.98	−0.88			
	Postimplantation loss						
L	−0.86	−0.51	−0.96	−0.78	−0.54	−0.77	−0.62 (0.29)
C		−1.22	−0.14	−0.62			
S			−0.24	−0.45			
	Live embryos						
L	2.17	1.36	2.56	2.03	1.52	1.86	1.64 (0.42)
C		2.27	0.65	1.43			
S			1.13	1.45			
	Embryonic survival (%)						
L	13.3	2.1	18.5	11.3	8.2	13.7	10.00 (3.4)
C		13.0	3.9	6.3			
S			14.8	12.4			

[a] Approximate SE computed from within cell variance

Table 5. Components of litter size from purebred and crossbred mothers mated to an unrelated strain: extract from analysis of variance[a]

Source	df	Mean squares			Live embryos	Embryo surv. %	Test vs[d]
		Corpora lutea	Preimplant. loss	Postimplant. loss			
Heterosis (Het)	1	18.57	9.79	20.64	143.57	6,224	Het × Bl
Het × Block (Bl)	2	10.34	10.77	11.01	26.12	1,062	Remain
SS × DS[b]	4	4.62	15.21	8.80	23.12	1,613	SS × DS × Bl[b]
SS × DS × Bl[b]	8	4.89	11.18	5.81	21.59*	1,194	Remain
Remainder[c]	243	4.873	7.451	5.203	9.913	648.7	

[a] Source, df and mean squares not shown for effects of secondary interest (total df = 67)
[b] Analysis of sire size (SS) × dam size (DS) interaction from ANOVA of crosses only, not independent of other effects shown
[c] Pooled between and within litter of birth of female (litter variance estimates were negative or very small)
[d] Error line used unless smaller than Remainder, when Remainder was used
* $P < 0.05$; ** $P < 0.01$

fixed and natural selection was effective in changing gene frequencies back nearer their original values. It is also notable that about one-third of the difference in 6-week weight when selection ceased had been lost by the time these crosses were made (Bhuvanakumar et al. 1985). Were it possible, a comparison of crosses then and now would have been interesting.

In terms of number born, purebred mothers bearing crossbred progeny had an increase of about 0.3 in litter size, a small increase due presumably to improved survival of the crossbred progeny. When the mother was crossbred rather than purebred, the increase in putative litter size at birth was about 1.6, approximately equally contributed by improved ovulation rate, re-

duced preimplantation loss and reduced post-implantation loss. This concurs with earlier studies in mice (Roberts 1960) and pigs (Sellier 1976) in which the benefits of line crossing or crossbreeding in reproductive rate are expressed primarily through improved performance of the crossbred dam.

The pattern of means of heterosis values when averaged over all crosses involving, for example, the large lines was rather confusing. Crosses of controls appeared to give the most heterosis for number of corpora lutea but the least for embryonic survival, such that differences in embryonic survival were not great. It is doubtful whether these effects reflect any more than sampling and the negative correlations introduced into the estimates of ovulation rate and embryonic survival by the method of recording. As with body size (Bhuvanakumar et al. 1985), there was no substantial difference in the extent of heterosis of the crossbred female depending on whether she was the result of mating of lines of different or of the same size. Thus the heterosis effects were explanable solely in terms of the drift of gene frequencies between the lines and were not increased by the differential selection.

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