Original article

Selection on testis size as an indicator of maturity in growing animals. II Correlated responses in reproductive rate

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Summary – Selection was undertaken in replicated lines of mice for 11 generations high and low on 5 wk body weight (HX, LX), on 5 wk testis weight (XH, XL), and on indices in which body and testis weight were selected in the same (HH, LL), and in opposite directions (HL, LH). There were correlated responses in number born in the 1st litter, with differences between pairs of lines averaged over replicates and the last 5 generations of: HX-LX = 2.2, XH-XL = 2.5, HH-LL = 1.0, HL-LH = −0.2, each with standard error of 0.6. The control mean litter size was 10.3. Differences were only partly removed by phenotypic correction for body weight, and limited data indicated that ovulation rate responded little more than litter size. Previous experiments suggesting that litter size can be changed by selecting on testis size are confirmed, but some of this response is associated with body weight change.

reproduction / growth / testis / selection / mouse

Résumé – Sélection sur la taille des testicules considérée comme un indicateur de la maturité des animaux en croissance. II Réponses corrélées sur les performances de reproduction. Une expérience de sélection chez la souris a été conduite pendant 11 générations, vers le haut (H) et vers le bas (L) selon plusieurs critères: masse corporelle chez le mâle à 5 semaines (lignées HX, LX); masse testiculaire à 5 semaines (XH, XL); indices combinant ces deux caractères, dans le même sens (HH, LL) ou en sens opposés (HL, LH). Chaque expérience a été répétée 2 fois. Des corrélations entre le nombre d'animaux nés en première portée et les critères cités ci-dessus ont été observées. En moyenne les différences entre lignées haute et basse ont été les suivantes, pour les cinq dernières générations: HX-LX = 2,2; XH-XL = 2,5; HH-LL = 1,0; HL-LH = −0,2; avec un écart type de 0,6. La taille de portée moyenne dans les 4 lignées témoins était de 10,3. Les différences ne sont que partiellement supprimées par une correction phénotypique tenant compte de la masse corporelle, et des données partielles indiquent que la réponse est légèrement plus élevée sur le taux d'ovulation que sur la taille de portée. Les résultats d'expériences antérieures suggérant que la taille des portées pouvait être modifiée par

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une sélection à partir de la taille des testicules sont confirmés, mais cette réponse est partiellement associée à une modification de la masse corporelle.

reproduction / croissance / testicule / sélection / souris

INTRODUCTION

It has been suggested that, because the same hormones are involved in gonadal development and pituitary response in both males and females, testis size of the male is an indicator of ovulation rate and thus litter size of his female relatives (Land, 1973). In a previous experiment with mice (Islam *et al*, 1976), selection on testis weight at 11 wks gave a correlated response in ovulation rate but not in litter size. Similarly, correlated response in testis size was obtained from selection for ovulation rate in pigs, but this was not associated with any substantial change in litter size (Cunningham *et al*, 1979; Johnson and Neal, 1988). Selection in sheep for juvenile testis size, corrected for body weight, led to little or no change in ovulation rate but to more pronounced responses in mature body weight (Land *et al*, 1980; Haley *et al*, 1989). Other workers have found some evidence of a correlation between testis size and litter size or ovulation rate in sheep (Ricordeau *et al*, 1979, 1986; Purvis *et al*, 1988), cattle (Toelle and Robison, 1985a) and pigs (Schinckel *et al*, 1983; Toelle and Robison, 1985b; see Haley *et al* (1989) for review). Selection for litter size in mice led to correlated changes in testis weight, even after adjustment for body weight (Eisen and Johnson, 1981).

The present experiment was designed to evaluate the efficacy of selection on testis size as an indicator of degree of maturity, with the aim of changing the relation between early growth rate and mature size. Selection was practised high and low on body weight, on testis weight, and on indices in which selection was practised in the same and opposite directions, all on mice of 5 wks of age. The responses in testis size and body weight at different ages are reported elsewhere (Hill *et al*, 1990). Because body size is itself correlated with both testis size and ovulation rate, this experiment provides an opportunity to clarify the relationships among the traits.

MATERIAL AND METHODS

The stocks used and basic design of the experiment are described in detail by Hill *et al* (1990). In summary, there were 8 selected lines and 2 unselected control lines, each replicated twice, maintained in 4 contemporary groups each of 4 selected lines (either all single trait or all index) and 1 control. Selection was practised for high or low body weight alone or males at 5 wks of age (lines designated HX, LX, respectively), for high or low testis weight alone of hemicastrated males at 5 wks of age (XH, XL), or for indices with both these traits selected in the same (index 1-HH, LL), or in the opposite directions (index 2-HL, LH) (Land *et al*, 1980; Lee and Land, 1985, Haley *et al*, 1989; Lee and Haley, 1990). Males were selected within full sib families and females were sampled at random within families, as were males of the controls (designated CC). There were 8 full sib families per line. Selection was undertaken on each generation, except 7, until generation 12, *ie* for 11 generations in all.

Litter size in first parity was recorded every generation on each family and on spare matings, usually a total of 12 in each line, and at generation 13 body weight at mating was recorded and more matings were set up. (Generation number in this paper refers to that of the offspring, *ie* litter size of generation 1 implies unselected dams mated to selected sires.) At generation 8, an extra group of females were taken for more detailed analysis, and at approximately 9 wks of age they were mated to males of the same line and observed daily for vaginal plugs. At d 17 of gestation (plug at d 0) these mice were sacrificed and the ovaries and uterus excised. Corpora lutea as an estimate of ovulation rate and the number of live foetuses were counted, and prenatal mortality calculated as their ratio (*ie* assuming all ova were fertilized).

Statistical analysis was undertaken as by Hill *et al* (1990). In essence the error variance was computed from the variation between replicates of lines selected in the same way. The error has only 8 degrees of freedom, but includes both drift variation between replicates and variation between mice within replicates.

RESULTS

The litter size of each generation during the period of selection is shown in figures 1 and 2, averaged over replicates. Individual replicate means are given in table I for the last few generations (9-12) as a simple summary of the responses, which includes most information since responses accumulate. Table I also contains estimates of litter size and body weight of the female at mating when recorded in generation 13. Contrasts among pairs of lines, *eg* HX-LX between the high and low body weight selected lines, are given in table II, which includes results pooled over generations 9-13. As lines had approximately the same effective population size, most inbreeding effects should be removed by comparing litter sizes of high and low lines.
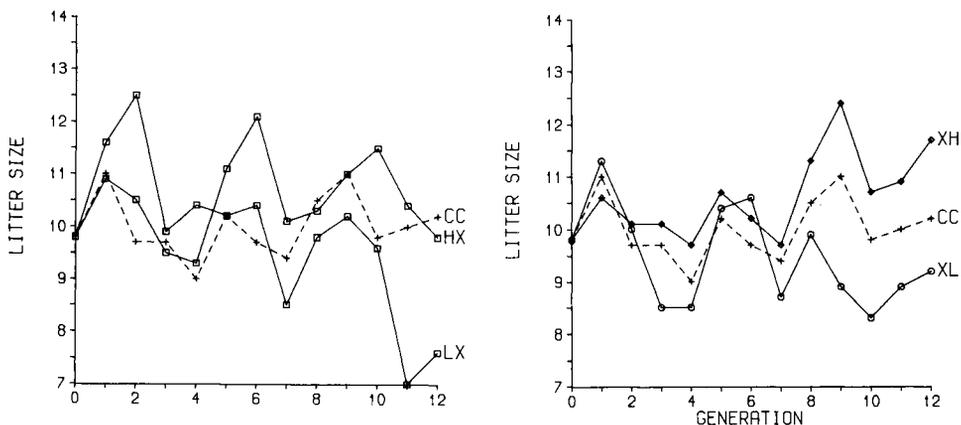

Fig 1. Litter size in first parity averaged over replicates: left graph, for lines selected on body weight (HX, LX), right graph for lines selected on testis weight (XH, XL), with their corresponding controls (CC).

Table I. Litter size (LS) averaged over generations 9-12 ($n = 81 - 94$ per line, summed over replicates) and at generation 13 ($n = 16 - 22$); mating weight (MW) at generation 13; number of failed matings (FM, of $n = 96$ matings made) summed over generations 9-12. [1]SE estimated from between replicate variance, except ( ) estimated from within line binomial variance.

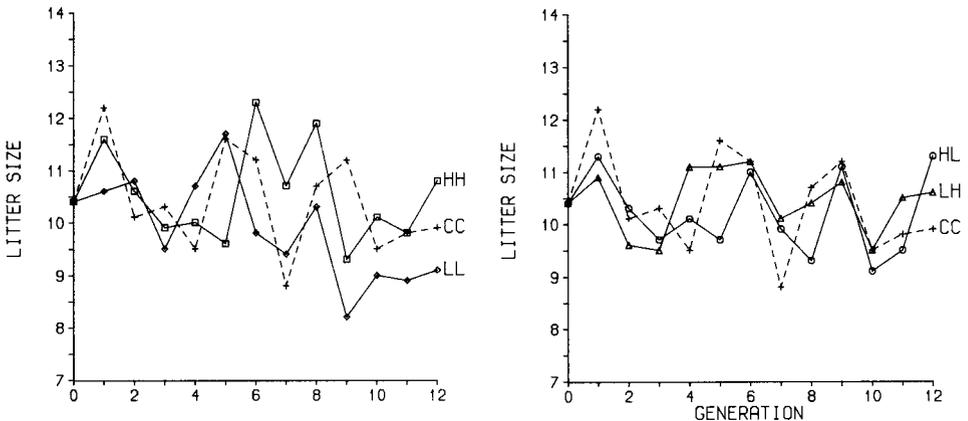| Generation Replicate Trait	9-12 average 1 LS	2 LS	Mean LS	13 Mean MW(g)	Mean LS	9-12 sum sum/96 FM
HX	11.3	10.0	10.7	28.0	11.2	3
LX	8.9	8.3	8.6	23.1	8.7	7
XH	12.4	10.5	11.4	29.4	11.4	5
XL	8.9	8.7	8.8	25.0	9.2	15
CC	10.9	9.6	10.2	27.6	10.7	9
HH	9.1	10.9	10.0	27.8	9.9	6
LL	9.0	8.6	8.8	24.1	9.5	11
HL	10.7	9.7	10.2	27.4	10.6	12
LH	11.1	9.6	10.3	24.0	11.0	4
CC	10.1	10.0	10.1	25.8	10.9	7
SE[1]			0.5	1.3	0.8	(2.7)[1]

Fig 2. As fig 1 but: upper graph for lines selected on index 1 (HH, LL), lower graph for lines selected on index 2 (HL, LH).

There was a consistent divergent response in litter size associated with selection on body weight alone (HX-LX = 2.2 born, averaged over generations 9-13, from table II), on testis weight alone (XH-XL = 2.5) and, although less, also on index 1 (HH-LL = 1.0) where the 2 traits were selected in the same direction. The response in litter size on the antagonistic indices (HL-LH = -0.2) was small. A difference of 2 mice is equivalent to about 20% of the mean, or 0.8 phenotypic standard deviations. Fitting a phenotypic regression on weight at mating reduced, but did not eliminate,

Table II. Contrasts of: litter size (LS) averaged over generations 9-13; litter size before (LS) and after (adj LS) adjustment for mating weight at generation 13; ovulation rate and live foetus number before (OR, LF) and after (adj OR, adj LF) adjustment for 5 wk body weight and prenatal survival at generation 8 (replicates pooled). *$P < 0.05$, **$P < 0.01$; [1] Generation 9-12 and 13 pooled from table I; [2] Litter sizes and mating weights given in table I; [3] Components of litter size and 5 wk weights given in table III; [4] HBW-LBW is the mean difference between all lines selected high and low on body weight, and similarly HTW-LTW for lines selected on testis weight.

Generations	9-13 LS[1]	13 LS[2]	13 adj LS[2]	8 OR[3]	8 LF[3]	8 PNS[3]	8 adj OR[3]	8 adj LF[3]
HX-LX	2.2**	2.5*	1.6	1.1	0.2	0.00	1.0	0.2
XH-XL	2.5**	2.2	1.4	1.7	1.9*	0.02	0.5	1.1
HH-LL	1.0	0.4	−0.3	2.6*	1.6	0.00	0.9	0.5
HL-LH	−0.2	−0.4	−1.0	0.8	−0.7	−0.10	0.4	−0.9
SE	0.6	1.1	0.9	1.2	0.9	0.08	1.1	1.0
HBW-LBW[4]	1.0*	0.8	0.1	1.5*	0.4	−0.03	0.8	−0.1
HTW-LTW	1.2**	1.0	0.7	1.2	1.4*	0.04	0.3	0.8
SE	0.3	0.6	0.5	0.7	0.5	0.05	0.6	0.5

the high-low contrasts, regardless of whether the lines had been selected on body weight or testis weight (table II).

Results of the more detailed study of components of litter size conducted earlier at generation 8 are given in table III, with contrasts summarised in table II. The differences in litter size (*ie* number of live embryos) were largest in the testis weight single (XH-XL) and index lines (HH-LL), and reduced but not eliminated by correction for body weight. The body weight (HX-LX) lines differed little in litter size or in body weight, the latter a quirk of this generation as responses were generally obtained (Hill *et al*, 1990). Ovulation rate differences were similar to or greater than those for litter size, and not completely removed by regression; but the HL-LH difference was positive for ovulation rate and negative for litter size. There was no obvious pattern in prenatal survival (table III).

Insofar as any trend was detectable in numbers of failed matings, these generally occurred in lines selected for low testis weight (table I).

DISCUSSION

It has been widely established that selection for body size in mice gives correlated responses in litter size (*eg* Falconer, 1973; Eisen, 1978) and similar results have been obtained in lines selected in this laboratory from the same base population (Brien *et al*, 1984). Evidence in other species is more equivocal: for example the genetic correlation between body size and litter size in pigs appears to be small (Legault, 1971; Morris, 1975), but there are few estimates. In our previous experiment in which selection was practised for testis weight at 11 wks, a positive correlated response in ovulation rate and body weight was obtained, but litter size increased in

Table III. Components of litter size at generation 8 (replicates pooled): Nos of mice mated (N_M) and pregnant (N_P), their 5 wk body weight (BW), ovulation rate (OR), No of live foetuses at 18 d of gestation (LF) and prenatal survival (PNS = LF/OR, computed for each mouse).

Line	N_M	N_P	BW(g)	OR	LF	PNS
HX	26	24	21.9	14.6	10.9	0.79
LX	29	28	21.8	13.5	10.7	0.79
XH	39	36	23.9	15.5	12.3	0.80
XL	32	32	21.4	13.7	10.4	0.78
CC	34	32	22.5	13.9	11.3	0.83
HH	30	28	25.0	15.7	11.8	0.76
LL	31	27	21.6	13.1	10.1	0.76
HL	14	12	23.3	14.7	10.0	0.67
LH	39	35	22.6	13.9	10.7	0.77
CC	33	32	22.5	14.1	11.5	0.82
SE			0.8	0.8	0.6	0.05

1 replicate and reduced in the other, with negligible mean change (Islam *et al*, 1976). No explanation other than sampling for this inconsistency between experiments, indeed between replicates, has been identified. Selection for ovulation rate in pigs has changed ovulation rate substantially, but not litter size (Cunningham *et al*, 1979; Johnson and Neal, 1988).

In the present experiment, positive correlated responses have occurred in litter size from selection on both 5 wk body weight alone and on 5 wk testis weight alone, leading to a divergence of some 20% of the mean in each case. Body weight and testis weight are, however, positively correlated, both phenotypically and, judging by most of our results (Hill *et al*, 1990), genetically. Our data on ovulation rate are much more scanty, but the indications are that it did not respond substantially more than did litter size because changes in embryonic survival were small. The HH, LL index lines showed less correlated response in litter size than the single trait lines, the HL, LH index lines almost none. The data from Hill *et al* and table II are summarized in table IV.

It is not easy to combine these results into a coherent whole. The relative correlated response in litter size (L) to selection on body weight (W) or testis weight (T) is, with equal selection intensities: $C_{LW}/C_{LT} = (r_{ALW}h_W)/(r_{ALT}h_T)$ where, for example, C_{LW}, r_{ALW} and h_w^2 denote the correlated response in litter size to selection on body weight, the genetic correlation of these traits and the heritability of body weight, respectively (Falconer, 1989). For the single trait selection, taking $h_W^2 = 0.26$ and $h_T^2 = 0.48$ from within family selection (Hill *et al*, 1990), $r_{ALW}/r_{ALT} = 1.2$. The other indication that both traits were similarly correlated is from the selection on index 2 (HL, LH), where little correlated response was observed in litter size. The smaller correlated response in litter size to HH, LL selection is surprising because the divergence between them in both body weight

Table IV. Summary of means and contrasts of selected traits in generations 10-12 and primiparous litter size in generations 9-13. [1]Generation 11 means only for CC, HX and LX testis weight which was not recorded in generations 10 and 12 of these lines. The body weights for generation 11 only were CC = 23.2 g, HX-LX = 3.4 g.

| | Males | | Females |
	5 wk body wt(g)	5 wk testis wt(mg)	Litter size
CC mean	23.1	57[1]	10.3
HX-LX	4.6	20[1]	2.2
XH-XL	4.0	37	2.5
HH-LL	3.4	31	1.0
HL-LH	3.6	−24	−0.2

and testis weight was similar to that in the single trait lines, but this could just be a sampling error (table II).

The overall conclusion from this experiment, which agrees with findings of Eisen and Johnson (1981), is that both body weight and testis weight influence litter size independently. In the accompanying paper (Hill et al, 1990) it was shown that selection for increased testis size in immature animals led to a small reduction in mature weight. This result, coupled with the increased litter size, suggests that selection for testis size can lead to increased female reproductive efficiency, as found by Lee and Haley (1990) with sheep, but that it should be regarded as a supplement to, rather than replacement for, direct selection on litter size.

ACKNOWLEDGMENTS

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