Selection for large and small litter size of the first three litters in mice

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Summary

A selection experiment based on female performance in 2 lines, L+ for increased and L− for decreased total number of young born alive in the first 3 births (TNY-3) was conducted for 8 generations. Line C, served as an unselected control. All litters were standardized to 8 mice. Responses and correlated responses were measured as a deviation from the control line. Heritability estimates for TNY-3 were 0.24 ± 0.10 from twice the dam-daughter regression and 0.13 ± 0.15 from the interclass correlations among half-sib families. After 8 generations of selection, the cumulated response was 3.80 young in the L+ line and — 3.44 in the L− line. Realized heritabilities for TNY-3 were 0.28 ± 0.05 in the L+ line, 0.21 ± 0.05 in L− line and 0.24 ± 0.03 for divergence. Realized genetic correlations were 0.82 ± 0.08 between TNY-3 and first litter size, 0.50 ± 0.12 between TNY-3 and second litter size and 0.60 ± 0.11 between TNY-3 and third litter size. Correlated responses per generation were 0.12 ± 0.07 g and — 0.22 ± 0.13 g for 6 week body weight in the L+ and L− lines respectively. Realized genetic correlations were 0.50 ± 0.13 between TNY-3 and 3-week body weight and 0.65 ± 0.04 between TNY-3 and 6-week body weight.

Key words : Mice, litter size, selection, heritability.

Résumé

Sélection divergente sur la prolificité chez la souris à partir des résultats des trois premières mises bas

Cette étude concerne une expérience de sélection sur la prolificité conduite chez la souris pendant 8 générations. Une sélection divergente (L+, L−) avec témoin (C) a été réalisée sur les performances des femelles (nombre total de nés vivants) lors de leurs 3 premières mises bas. La taille des portées était standardisée à 8 après la mesure de celle-ci. Les réponses directes et corrélées à la sélection ont été mesurées à partir des écarts à la lignée témoin. La réponse à la sélection après 8 générations était de 3,80 nés dans la lignée haute (L+) et — 3.44 dans la lignée basse (L−). L'héritabilité du nombre de nés totaux (TNY-3) a été estimée à $0,24 \pm 0,10$ par le double de la régression mère-fille et $0,13 \pm 0,15$ à partir de la corrélation entre demi-germains. Pour ce même caractère, la valeur réalisée était de $0,28 \pm 0,05$ dans la lignée haute (L+), $0,21 \pm 0,05$ dans la lignée basse (L−) et

0,24 ± 0,03 sur les écarts entre ces 2 lignées. Les réponses corrélées par génération sur le poids à 6 semaines étaient de 0,12 ± 0,07 g et — 0,22 ± 0,13 g dans les lignées haute et basse respectivement. La corrélation génétique réalisée entre le nombre total de nés et la prolificité aux 1res, 2es et 3es mises bas a été estimée à 0,82 ± 0,08 ; 0,50 ± 0,12 et 0,60 ± 0,11. Entre le nombre total de nés et le poids, elle était de 0,50 ± 0,13 et 0,63 ± 0,04 à 3 et 6 semaines respectivement.

Mots clés : Souris, taille de portée, sélection, héritabilité.

I. Introduction

Litter size is a quantitative character of considerable complexity, determined by ovulation rate, zygotic survival, implantation, embryonic viability, parturition and post-partum survival of the young (ROBERTS, 1965). Many selection experiments for litter size in mice have been carried out (FALCONER, 1960 b ; DALTON & BYWATER, 1963 ; BATEMAN, 1966 ; BRADFORD, 1968 ; EKLUND & BRADFORD, 1977 ; BAKKER et al., 1978 and EISEN, 1978), but in all of them the selection criterion was litter size at first parity. However, litter size at first birth may not be representative of litter size at subsequent parities. Selection for first litter size increases litter size at first birth, but with a permanent breeding method (i.e. males left continuously with females), litters are not increased at subsequent births (WALLINGA & BAKKER, 1978). No selection experiments have been reported for fertility based on the size of several litters. In the present study selection was based on the number of young born alive in the first 3 births in mice, to compare it with selection experiments for litter size at first birth. The genetics of litter size in mice and multiparous farm livestock (rabbit, pigs) is similar. Besides, the improvement of prolificacy in the latter is generally based on several births. Thus the results of this experiment could be considered as predictors of possible results in farm livestock.

The objectives of the present study were : a) to determine the realized heritability of litter size (TNY-3) ; b) to evaluate the efficiency of selection for prolificacy based on total litter size of the first 3 births, and c) to evaluate the correlated responses and realized genetic correlations of reproductive traits with body weight. Selection for litter size is known to affect body weight through its correlation with ovulation rate (KENNEDY & KENNEDY, 1972).

II. Materials and methods

The mice used in this experiment came from a non-inbred population of the NMRI strain. This base population (150 pairs) was divided into 3 lines, L+, L− and C, with 50 pairs per line. Individual selection based on the number of young born alive in the first 3 births (TNY-3) was conducted in 2 lines, L+ for increased fertility and L− for decreased fertility. Line C, an unselected control, was used to adjust for possible environmental changes. The 3 lines were maintained with 50 mating pairs per generation. A mating system of maximum avoidance of inbreeding was applied in line C where one male and female were randomly chosen from each litter.

Individual selection in L+ and L− lines was conducted only for females. Males were randomly selected. Females which did not produce 3 litters in a period of 85 days were not considered for selection. This study included 8 generations of selection. In each generation, the best 13-17 females in each selected line were chosen. First litter progeny from the selected females provided the 50 females and 50 males constituting the next generation. Males and females were pair-mated randomly at 50 to 60 days of age with the avoidance of full-sib mating. One female and one male were cohabited countinuously during a period of 85 days. Mice were mated on the same day in order to synchronize the 1st birth in each generation, avoiding the female age effect on litter size in the next generation (KENNEDY & KENNEDY, 1972).

At 2 days of age, the number of young was recorded and litters were standardized to 8 young, attempting to obtain 4 males and 4 females. Addition of young was made in litters with less than 8 young from litters of the same age and line. After weaning at 19 days of age, males and females were maintained separately. All mice were weighed individually at 3 and 6 weeks of age. Body weight is presented as the unweighted mean of males and females.

The management and environmental conditions in the animal house were similar for lines across generations. Temperature was kept at $21 \pm 1\,°C$ with a lighting cycle of 12 hours light - 12 hours dark. The mice were fed SANDERMUS pellets *ad libitum.*

Estimates of genetic parameters. Heritabilities were estimated in the base population by 2 methods : a) from twice the regression of daughter on dam and b) from 4 times the intraclass correlation of half-sibs. Forty half-sibs families were analyzed. The family size was 4 dams per sire and 4 daughters per dam (ROBERTSON, 1959).

Variance components were estimated in a nested analysis of variance with unequal subclasses. The statistical model was :

$$Y_{ijk} = \mu + S_i + D_{j(i)} + e_{ijk}$$

where Y_{ijk} is the record of the kth progeny of the jth dam mated to the ith sire ; μ is the mean ; S_i is the effect of ith sire ; $D_{j(i)}$ is the effect of the jth dam mated to the ith sire and e_{ijk} is the residual.

Variance components and standard errors of heritabilities (h^2) were calculated following the formulae of BECKER (1967). The realized heritabilities for L+, L− and divergent selections were calculated by doubling the regression coefficient of direct response (R) on cumulative selection differencial (SDa) up to generation 8 (FALCONER, 1960 a). The realized selection differential (SDr) was calculated by weighting the litter size of each dam by the number of daugthers that survived till mating. The expected selection differential (SDe) was calculated as the difference between the average TNY-3 of selected females and the average TNY-3 of all the females at each generation. Standard errors of realized heritabilities were based on formulae of HILL (1972 a, 1972 b).

Realized genetic correlation between 2 traits, when only one of them has been selected, was calculated using the formulae of RUTLEDGE *et al.* (1973) :

$$r_{Gr} = b_{CR/R} (h_x \sigma_{Px}/h_y\ \sigma_{Py})$$

where $b_{CR/R}$ is the realized genetic regression of correlated response in trait y on direct response in trait x. Standard errors of r_{Gr} were calculated using the formulae of HILL (1971).

III. Results

A. *Base population characteristics*

Before the selection experiment for fertility was started, phenotypic and genetic parameters of reproductive and body weight traits were estimated to predict the correlated and direct response to selection. These estimates also were used to decide on appropriate selection procedures. Means, phenotypic variances and coefficients of variation of reproductive traits estimated in the base population are shown in table 1.

TABLE 1

Reproduction traits in the base population, NMRI strain.

Caractéristiques de reproduction de la population fondatrice, souche NMRI.

Trait	Sample size	Mean	Phenotypic variance	Coef. of variation
1st litter size (FLS)	155	11.35	9.24	0.26
2nd litter size (SLS)	125	12.62	14.44	0.30
3rd litter size (TLS)	75	12.62	9.30	0.24
TNY-3*	75	35.07	37.75	0.18
Cohabiting to 1st birth (days)	155	22.61	30.24	0.24
1st to 2nd birth (days)	125	22.68	36.30	0.27
2nd to 3rd birth (days)	75	26.03	42.51	0.25

* Total number of young born in the first 3 births.

Females used for breeding remained together (8 females in each cage) from weaning to mating. This system produced synchronization of the 1st estrous cycle. The 87 p. 100 of females had their 1st litter in a period of time between the 19th and the 24th post-mating day. The synchronization for the 2nd and 3rd parities was 83 p. 100 and 69 p. 100 respectively.

Estimates of heritabilities for litter size from daughterdam regression coefficients and from half-sib correlations are given in table 2. Heritability estimates for TNY-3 based on regression coefficients (2 b) were obtained with lower error and were comparable to realized heritabilities obtained by actual selection. Heritability estimates of first litter size were higher than h^2 of 2nd litter size. The heritability of the trait « total of several litters » was calculated following the formula given by BOLET & LEGAULT (1982) based on repeatability (t), h^2 in each litter and number of litters (n) :

$$h_s^2 = nh^2/[1 + (n - 1)t]$$

The estimate of heritability for TNY-3 obtained by this formula was 0.26 ± 0.10 which was similar to 0.24 ± 0.10 and 0.24 ± 0.03, calculated from « 2 b » and the h_r^2 after the 8 generations of selection, respectively.

TABLE 2

*Estimates of heritability ± S.E. from daugther-dam regression (2 b)
and the intraclass correlation among half-sib families (4 t).*

*Estimation de l'héritabilité à partir de la régression mère-fille (2 b)
et de la corrélation entre demi-frères (4 t).*

Trait	Method	
	4 t ± S.E.	2 b ± S.E.
1st litter size	0.21 ± 0.17	0.12 ± 0.08
2nd litter size	0.11 ± 0.13	0.10 ± 0.09
3rd litter size	0.07 ± 0.20	0.13 ± 0.10
TNY-3	0.13 ± 0.15	0.24 ± 0.10

B. *Selection differential*

Realized selection differentials (SDr) and expected selection differentials (SDe) are shown in table 3. SDr decreased across generations and was very low in the 7th and 8th generations. SDe was higher than SDr. The difference between SDe and SDr was small in the L+ line (40.00 — 39.35), but it was larger in L− (36.86 — 32.12). This difference (4.74) in the L− line was due to a small litter size : fewer females were chosen from selected litters.

TABLE 3

Selection differential of number of young born in the 3 first litters.

Différentielle de sélection pour le nombre de nés vivants aux 3 premières mises bas.

Generation		1	2	3	4	5	6	7	8
L+	SDr	6.97	5.54	7.07	5.94	3.02	4.31	4.21	2.29
	SDe	6.93	6.36	6.70	5.90	3.83	4.19	3.73	2.41
L−	SDr	— 4.89	— 4.68	— 6.11	— 4.20	— 3.38	— 4.00	— 2.75	— 2.11
	SDe	— 5.71	— 6.22	— 7.02	— 5.41	— 3.29	— 3.69	— 2.95	— 2.60

SDr : Realized selection differential.
SDe : Expected selection differential.

The selection intensity based on the percentage of females selected was low in both lines : 0.81 in the L+ line and 0.68 in the L− line. The contributions of each parity to SDr are shown in table 4. In the early generations of selection, the contribution was similar among parities, but from the 5th generation on the contribution of the 3rd parity was lower than the others.

TABLE 4

Contribution of each parity to the selection differential *.

Contribution de chaque mise bas à la différentielle de sélection.

Line	Parity	Generation								
		1	2	3	4	5	6	7	8	
	1st	1.63	0.68	2.66	2.06	2.29	2.02	1.60	1.86	41 %
L+	2nd	1.84	1.92	1.16	2.29	1.03	1.41	1.63	0.74	29 %
	3rd	1.89	2.88	3.62	1.65	0.42	0.06	0.40	0.20	30 %
	1st	1.89	0.51	1.86	1.94	1.78	2.01	0.87	1.90	33 %
L−	2nd	1.85	2.07	2.36	2.35	0.74	2.32	2.31	1.85	42 %
	3rd	2.50	2.45	2.16	1.16	0.73	0.06	0.55	— 0.20	25 %

* Estimated as the difference between the average litter size for each parity of selected females
   and that of all females, in each generation.

C. Direct response and realized heritability

The changes in TNY-3 mean over generations in the L+, L− and C lines are
presented in figure 1. The changes in TNY-3 mean in theses lines over generations
were due to the effects of selection plus fluctuated environments. Direct response to
selection (R) in each line, and cumulated response (Ra) and SDa for the divergence,
are given in table 5. After 8 generations of selection, the Ra was 3.80 young born in
the L+ line and — 3.44 in the L− line when expressed as deviations from the
control line.

TABLE 5

Response *, selection differential and realized heritability.

Réponse à la sélection, différentielle et héritabilité réalisée.

Generation	Line				
	L+	L−	Divergence		
	R.	R.	Ra.	SDa.	$h_r^2 \pm$ S.E.**
1	— 3.05	— 2.30	— 0.75	11.68	
2	3.58	— 0.67	3.50	22.08	
3	2.04	1.20	3.97	35.26	0.27 ± 0.07
4	0.71	1.34	3.71	45.40	0.21 ± 0.05
5	0.10	— 2.07	5.88	51.80	0.23 ± 0.04
6	1.38	— 0.32	7.58	60.11	0.25 ± 0.04
7	— 2.86	— 3.87	8.59	67.07	0.26 ± 0.03
8	1.90	3.25	7.25	71.47	0.24 ± 0.03

*   Expressed as deviations from the control line.
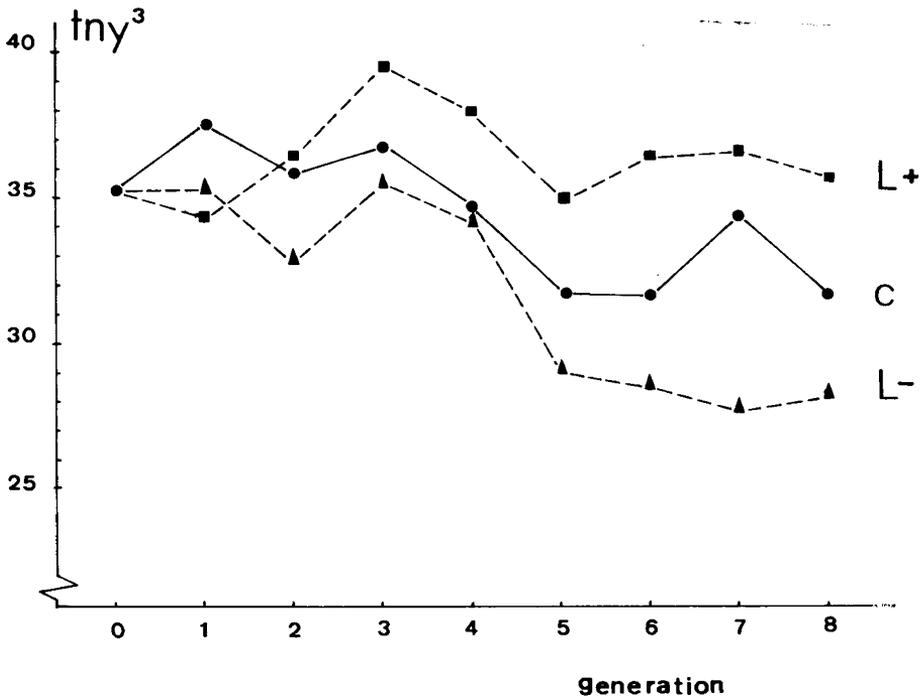** The h_r^2 was calculated by doubling the regression coefficient of R. on SDa.

FIG. 1

Mean for TNY-3 in L+, L− and C line.

Evolution du TNY-3 dans les lignées L+, L− et C.

The realized heritability for the TNY-3 was 0.24 ± 0.03 for the divergence between L+ and L− lines when estimated with the data from 8 generations of selection. Realized heritabilities for the divergence, estimated every generation up to generation 8, are given also in table 5. Realized heritability was 0.28 ± 0.05 for the L+ line and 0.21 ± 0.05 for the L− when estimated using the data from 8 generations.

D. Correlated response to selection and realized genetic correlation

1. Between TNY-3 and 1st, 2nd and 3rd litter size

The means of the 1st (FLS), 2nd (SLS) and 3rd (TLS) litter for the L+, L− and C lines in the 8 generations of selection are given in table 6. Correlated responses per generation for litter size at 1st, 2nd and 3rd parity were 0.18 ± 0.11, 0.22 ± 0.07 and 0.28 ± 0.07 in the L+ line and 0.18 ± 0.11, 0.13 ± 0.06 and 0.01 ± 0.07, respectively in the L− line. The realized genetic correlations (r_{Gr}) between the TNY-3 and the FLS, between TNY-3 and the SLS, and between TNY-3 and the TLS were 0.82 ± 0.08, 0.50 ± 0.12 and 0.60 ± 0.11, respectively (table 8).

TABLE 6

Mean of litter size of the 1st, 2nd and 3rd parity in the L+, L− and C line.

Prolificité des lignées L+, L− et C lors des 3 premières portées.

Line	Litter	Generation								
		0	1	2	3	4	5	6	7	8
	1st	11.35	13.06	12.65	12.49	11.33	9.53	12.09	11.11	11.07
C	2nd ...	12.59	12.83	12.13	12.92	12.43	11.65	10.71	10.91	10.90
	3rd ...	12.62	11.37	11.09	11.94	10.89	9.52	10.00	10.42	9.75
	1st	11.35	12.22	12.71	12.60	12.09	12.18	12.89	11.36	11.98
L+	2nd ...	12.59	12.00	12.39	13.51	13.28	12.32	11.50	13.09	11.68
	3rd ...	12.62	10.35	10.90	13.07	12.21	10.21	11.87	11.76	—
	1st	11.35	12.63	11.27	11.07	11.06	10.20	10.74	8.77	9.27
L−	2nd ...	12.59	12.13	11.62	12.79	11.21	10.13	10.39	10.04	9.36
	3rd ...	12.62	10.23	11.03	12.14	11.20	9.56	8.48	9.93	9.76

After several generations changes were found in the phenotypic correlations (r_P) among the size of the 1st, 2nd and 3rd litters. Phenotypic correlations in the base population and those of the selected lines in generation 7 are given in table 7. The selection resulted in increased phenotypic correlations between the size of the 1st and 2nd litter, but r_P between the size of the (1st + 2nd) litter and the 3rd one was negative.

TABLE 7

Phenotypic correlations among litter size.

Corrélations phénotypiques entre les tailles de portée aux 3 premières mises bas.

Litter size	Line L+*	Line L−*	Base population
1st - 2nd	0.48	0.38	0.07 ± 0.07
2nd - 3rd	— 0.18	— 0.04	0.11 ± 0.11
1st - 3rd	— 0.13	— 0.39	0.02 ± 0.06
(1st + 2nd) - 3rd	— 0.25	— 0.23	0.14 ± 0.10
* Selected line at generation 7.			

2. *Between TNY-3 and body weight*

To study the correlated responses in body weight, 3 traits were analysed : 3 and 6 week body weights and 3-6 week body weight gain. Regression of the divergence between L+ and L− means on generations showed an average increase per generation of 0.08 ± 0.32 g and 0.14 ± 0.04 g for 3-week body weight and 3-6 week body

weight gain, respectively. Correlated responses per generation for 6-week body weight were 0.12 ± 0.07 g and -0.22 ± 0.13 g in the L^+ and L^- lines, respectively. Realized genetic correlations are given in table 8.

TABLE 8

Realized genetic correlations between TNY-3 and other traits.

Corrélation génétique réalisée entre le nombre total de nés et d'autres caractéristiques.

Traits	$r_{Gr} \pm$ S.E.
1st litter size	0.82 ± 0.08
2nd litter size	0.50 ± 0.12
3rd litter size	0.60 ± 0.11
3-week body weight	0.50 ± 0.13
6-week body weight	0.65 ± 0.04
Gain 3-6 week	0.26 ± 0.14

IV. Discussion

A. *Estimation of heritability*

Heritability estimates for litter size decreased with litter order. That is in agreement with the results of some studies in pigs (BOLET & FELGINES, 1981), (JOHANSON & KENNEDY, 1982). It seems that relative to the size of 1st litters the sizes of 2nd and 3rd litters are more influenced by environmental factors such as interval between litters, number of young born in the previous parity, etc. On the other hand, the heritability estimate for TNY-3 was higher than that for each parity. This agrees with the results obtained under a permanent breeding system as given in this study, e.g. NAGAI & YOKOYAMA (1982) who obtained an estimate of 0.40 for the number of young born during a period of 200 days and 0.32 for the average of litter size per parity, and STRANG & KING (1970) who found a higher heritability as the number of litters included in the estimation increased in swine.

B. *Selection differential*

One of the problems that appeared in the selection process for the TNY-3 was the impossibility of exerting large selection pressure. The selection intensity (i) in the L^+ line (0.81) was low when compared with that obtained by BAKKER *et al.*, (1978) who selected for 1st litter size (1.54) without standardizing number of young and, thus having more offspring available *per dam*. Besides, the low selection differential in our experiment was caused by the procedure that females that did not produce 3 births during 85 days were discarded. The percentage of females discarded was not very high for the 1st few generations, but increased through the later generations causing a gradual decrease in SDr in the selection process. A reduction

in the contribution of the 3rd litter to DSr was also observed. One possible cause of the lower contribution of the 3rd litter is that the permanent breeding system causes a greater stress in some of the females that reach the 3rd parity.

C. *Selection response and realized heritability*

The response of TNY-3 was variable through the 8 generations and negative response were obtained in some generations. This result was due to the small number of females used for each generation (50 females per line), and to the low DSr.

The h_r^2 obtained after 8 generations of divergent selection was 0.24 ± 0.03, which is higher than that found in most of selection experiments by the litter size of the 1st parity : 0.14 ± 0.02 (FALCONER, 1960 b) ; 0.06 ± 0.02 (DALTON & BYWATER, 1963) ; 0.16 ± 0.06 (EKLUND & BRADFORD, 1977). This could be explained by the fact that in all of these experiments a larger number of generations (12-29) was used. The factors that may have influenced the h_r^2 estimate are :

1. *Litter size standardization*

Prolificacy selection without standardizing the litter size is less effective. Maternal effects may be negatively correlated to direct genetic effect in mice and the other multiparous species (VANGEN, 1981). Standardizing litter size at birth is a way of overcoming the difficulty due to maternal effects (OLLIVIER, 1982). FALCONER (1960 b) and BAKKER *et al.* (1978) did not standardize the litter size and obtained a h_r^2 of 0.14 ± 0.02, 0.11 ± 0.02 respectively.

2. *Trait by which the selection is performed in order to improve the litter size*

STRANG & KING (1970), BOLET & LEGAULT (1982) and OLLIVIER (1982) reported in swine that h_r^2 increases as the number of parities increases, especially when repeatability is low. MATHERON (1982) who selected for litter size of 3 parities in rabbit, obtained a realized heritability (0.22 and 0.25) similar to that found in our experiment. We assume that in mice and other multiparous species, some of genes influencing the size of each litter are different since the genetic correlations between then are not high.

3. *Age at mating*

The age at mating influences the prolificacy and the selection effectiveness through body weight and the ovulation rate (KENNEDY & KENNEDY, 1972). When mice are mated at an early age ovulation rate is a limiting factor of 1st litter size while the uterine capacity is critical in the following litters (FINN, 1963). Improved ovulation rate does not increase litter size (BRADFORD, 1969). In our experiment, mice were mated at a later age (50-60 days) when females were fully mature : our NMRI strain is quite percocious.

4. *Number of selection generations in which the h_r^2 is calculated*

BRADFORD (1968), in a selection experiment to improve the 1st litter size, obtained after 8 generations of selection a h_r^2 of 0.25 ± 0.05 (similar to the one we obtained

with the same number of generations), and of 0.13 $\pm$ 0.07 and 0.22 $\pm$ 0.06 after 11 generations (in 2 replicates). The selection response decreased with generations, because of the progressive decrease of the additive genetic variation of this trait. In all experiments selecting for 1st litter size, an association between h_r^2 and number of generations with response exists. In this way, when selection is very effective, the h_r^2 is high and the response subsists during a few generations (BRADFORD, 1968 ; EKLUND & BRADFORD, 1977). On the other hand, if h_r^2 is low, the response continues for more generations of selection (FALCONER, 1960 b ; BAKKER et al., 1978 and DALTON & BYWATER, 1963). The conclusion of that is the little variability of fertility, since most of the additive genetic variation had been fixed by the effect of the natural selection on the reproductive capacity.

5. Direction of selection

The heritability in L$^+$ line, (0.28 $\pm$ 0.05) was higher than that of the L$^-$ line (0.21 $\pm$ 0.05). The result is not in good agreement with that of FALCONER (1960 b) who obtained a higher h_r^2 in the L$^-$ line (0.23 $\pm$ 0.02) than in the L$^+$ line (0.08 $\pm$ 0.02), after 20 generations of divergent selection for 1st litter size. This difference may have been due to the fact that we have selected indirectly for fecundity improvement in both lines, since we only make the selection among those females that in a period of 85 days have given 3 litters. Fertility could be correlated with litter size and made negative selection less effective. This effect is not detected in FALCONER's experiment selecting for the 1st litter size, whereas it was observed in our experiment selecting for the first 3 litters.

D. Correlated response in reproductive traits

Selection for TNY-3 modified the size of each litter in a different degree when the females were subjected to a permanent breeding method. Selection gave response in the 1st and 2nd birth and that increment caused an environmental effect (negative in the L$^+$ and positive in the L$^-$ lines) on the 3rd litter size. This effect was also detected by WALLINGA & BAKKER (1978) who selected females under permanent breeding system to increase litter size in the 1st birth. They found a decrease in size of the 2nd and 3rd litters while the control line was unchanged. WALLINGA & BAKKER (1978) and FINN (1963) considered that the decrease was resulted from overloading in the uterus, as seen by the embryonic mortality, to maintain large litters. HARKNESS (1956) and KAO et al. (1962) showed that the synthesis of collagen is the limiting factor.

The disadvantage of selection for the 1st litter size is that the improvement of this 1st birth is not maintained in the following ones and at the same time a reduction in lifetime reproduction occcurs (LUXFORD & BEILHARZ, 1982 and SCHÜLER & BÜNGER, 1982). LUXFORD & BEILHARZ (1982) selected 2 lines (A and B) of mice at 1st parity for total litter weight at birth and for the number of young alive respectively. For each selected line a response was obtained but, overall lifetime reproduction was reduced in both lines, for the selected traits.

In our experiment the increment due to selection for TNY-3 was not large, but this response remained positive in the size of the 2nd and 3rd litters. Selection for the 1st litter size acts through the changes in ovulation rate and embryonic mortality (FALCONER, 1960 b), but the ovulation rate increase only affects the 1st litter size and not the following ones (BRADFORD, 1969). The limiting factor of 2nd, 3rd and following

litter sizes is not only the ovulation rate but also the uterine capacity, in the multiparous species (VANGEN, 1981), which controls litter size through embryonic mortality, particulary in a permanent breeding system (WALLINGA & BAKKER, 1978). Selection for the 1st litter size does not always improve uterine capacity. Selection for the size of several litters has the disadvantage that selection pressure is smaller. However this effect could be counteracted in livestock breeding by increasing the population size.

From these results we can conclude that for improving prolificacy in multiparous species without reducing the reproduction lifetime, either the amount of young born in a period of time or the total number of young born in several litters should be considered. According to BOLET & LEGAULT (1982) a selection index should be used with the size of several litter, especially when the phenotipic correlation between them is not high.

E. Correlated response in body weight

Litter size may have influenced body weight through its correlation with ovulation rate. The change in litter size may be due to a modification in ovulation rate (in this last case there would also be changes in body weight). The r_{Gr} between TNY-3 and 3-week body weight was high (0.05 ± 0.13) and also between TNY-3 and 6-week body weight (0.65 ± 0.04). BAKKER et al. (1978) and FALCONER (1960 b) did not find significant changes in body weight when selecting for the 1st litter size, but JOAKIMSEN & BAKER (1977) obtained a r_{Gr} of 0.6 and EISEN (1978) obtained a r_{Gr} of 0.52 ± 0.10. That is in good agreement with our results. A lack of correlated response in body weight (FALCONER, 1960 b), could be explained by the fact that the litter size was not standardized to remove the negative environmental correlation between litter size and body weight.

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