Theor. Appl. Genet. 51, 119-125 (1977)

The Relative Importance of Prenatal and Postnatal Maternal Influences on Growth in Mice

H. Brandsch and A.E.H. Kadry
Fachgruppe Haustiergenetik und Tierzüchtung, Sektion Tierproduktion und Veterinärmedizin, Karl-Marx-Universität, Leipzig (DDR)

Summary. The cross-nursing technique was used to assess the relative importance of prenatal and postnatal maternal influences on growth in mice from an unselected population originated from a cross of four highly inbred strains. Body weights were studied at birth, 7-, 14-, 21- and 42-days, in addition to the weight gains between these ages and tail length at 21 and 42 days of age. At littering, each dam in each nursing set retained two of her own offspring and two were transfereed to each of the other dams in the set, so that each nursed litter contained six young representing three mothers. Prenatal influences accounted for 37, 15, 10, 11 and 13% of the total variation in the respective body weights, while postnatal influences accounted for 0, 64, 65, 49 and 14% at the respective ages. In the case of weight gains, prenatal influences were responsible for 16, 4, 6 and 30%, while postnatal influences were responsible for 66, 66, 31 and 7% of the total variation in gain during the respective four periods examined. Apparently the individual weight gain from 7 to 14 days was a better measure of the lactational performance of the dam than individual 14-day weight. For tail length, prenatal influences accounted for 6% and 4% of the total variation in tail length at 21 and 42 days, respectively, while postnatal influences accounted for 60% and 24% at the respective ages. Generally, there was no indication of an important interaction between the nurse and the nursed young at any stage studied.

Key words: Mice - Cross-nursing Technique - Body Weight - Prenatal and Postnatal Maternal Influences

Introduction

Maternal influences are an important source of variation in mammalian species. The maternal environment provided by the female may be split into two major, phases, i.e. the prenatal (the period from ovulation to parturition) and the postnatal (the period from parturition to weaning). Cox and Willham (1962) reported that experimental designs utilizing planned nursing schemes provide one approach to problems concerning maternal influences on quantitative traits. Legates (1972) reviewed generally the role of laboratory animals in the study of maternal influences, and the usefulness of the cross-nursing technique to separate experimentally prenatal and postnatal maternal influences and to assess their relative importance on growth. Many workers reported experiments with mice where cross-nursing technique was used to study the role of maternal influences on growth traits (e.g. Bateman 1954; Cox et al. 1959; Young et al. 1965; El-Oksh et al. 1967; Nagai 1971; Rutledge et al. 1972; La salle and White 1975; Nagai et al. 1975). However, the need persists for further examination of relative changes with age of prenatal and postnatal maternal influences on growth in mice since many of the previously cited studies used similar genetic stocks.

The present study was undertaken to assess the relative importance of prenatal and postnatal maternal influences upon body weight and weight gains from birth to six weeks of age and on tail length measured at 21 and 42 days of age in mice.

Material and Methods

Source of data and laboratory procedures:

The mice used in the present study came from an unselected base population. This population was formed by crossing four highly inbred strains of mice, namely: AKR/Bln.; AB/Jena; A/J Han Jena and H/ADW (which were maintained by brother-sister mating for about 50 to 150 generations at LVS Probstheida, Karl-Marx-University, Leipzig), followed by 5 generations of random mating using approximately 20 sires and 40 dams per generation. Fifty one males (7 to 8 weeks old) and 153 contemporary females were randomly chosen from the base population and matings made among them. The mating ratio was one male to three females, avoiding full and half sibbing, and no two sisters or half sisters were mated to the same sire. Pregnant females were placed in separate

cages approximately 17 days post mating and checked twice daily for newborn litters. Only first parity litters were used. At parturition the young mice were arranged in cross-nursing sets of three litters each according to the following restrictions: a.) The three litters should be born within the same 12 hour period; b.) Each litter should contain at least six mice (litters having fewer than six mice were excluded); c.) Each sire should be represented by only one litter in a given cross-nursing set; d.) No two sisters or half sisters should have their litters in the same cross-nursing set; e.) The sires of the three litters should not be related to one another or to either of the three dams. Newborn litters were sexed as accurately as possible, standardized to six, and each mouse was permanently identified by toe clipping. The remainder of the young were discarded. Individual birth weights were taken while sets were being established, within approximately 12 hours after the litters were born. Each dam was then given randomly two of her own young and two from each of the other two dams in her set. An attempt was made to ensure that both sexes were represented in each pair. Individual weights were taken again at 7-, 14- and 21-days of age to the nearest 0.1 gram. At 21 days the young were weaned and segregated by sex into separate cages, with postnatal litter mates occupying the same cage. The final weighing was made at 42 days of age. Tail lengths were measured to the nearest 0.1 cm. at 21 and 42 days of age. In addition, the amount of gain made during the respective periods, namely from birth to 7 days, from 7 to 14 days, from 14 to 21 days and from 21 to 42 days of age, were obtained. Tap water and a standard commercially prepared pelleted ration (Mäuse- und Rattenfutter, R 09) were supplied ad libitum. The laboratory was maintained at approximately 22°C and 60% relative humidity with a continuous light to darkness ratio of 12 hr. light to 12 hr. darkness.

Statistical Procedures

Prior to analysis the data were adjusted for sex differences by using a multiplicative correction factor similar to that described by Falconer (1953).

The mathematical model used in the statistical analysis of the data was identical to the one used by Cox et al. (1959) and described by Legates (1972) as follows:

$y_{klm} = \mu + a_k + p_l + (ap)_{kl} + e_{klm}$; where y_{klm} is the measured trait taken on the m^{th} young belonging to the 1^{th} litter as reared and k^{th} litter as born, μ is the general mean of the set, a_k and p_l are the effect of the k^{th} actual (prenatal) and 1^{th} nurse (postnatal) mothers, respectively, $(ap)_{kl}$ is the interaction of the prenatal and postnatal effects and e_{klm} is the effect of differences among litter mates (full sibs) born and reared alike. Assumptions were made that the a_k, p_l, $(ap)_{kl}$ and e_{klm} are independent random variables, each with mean zero, and with variances σ_a^2, σ_p^2, σ_{ap}^2 and σ_e^2, respectively. Genetic interpretation of the various effects have been given by Cox et al. (1959), Rutledge et al. (1972) and Legates (1972).

Results and Discussion

Body Weights

Table 1 shows the mean squares, components of variance and the percentages they represent of the total variance in body weights studied. Prenatal influences were highly significant ($P < 0.01$) for all weights examined. They were important for birth weight accounting for 37% of the variance in this trait, but they were responsible for only 15%, 10% and 11% of the variance in weight at 7-, 14- and 21-days of age, respectively. At 42 days, the prenatal effects accounted for 13% of the total variance in individual body weights at this age. The prenatal component of variance includes the genetic and uterine effects that cause litter mates to be more alike than mice from different litters. Therefore, it was expected that this component and the error component would include almost all the variation in birth weight. Thereafter, in spite of the observed decline, prenatal influences were still highly significant ($P < 0.01$) until 42 days of age (Table 1). Similar results were reported by Cox et al. (1959) and Young et al. (1965). They found that prenatal effects accounted for 38%, 6 to 12% and 18% of the total variance in birth weight, 21- and 42-day weight, respectively. El-Oksh et al. (1967), Nagai (1971) and Rutledge et al. (1972) reported that prenatal influences were responsible for 61%, 52% and 50%, respectively, of the variance in birth weight. The descrepancy between these estimates and the present one may be explained by strain differences, since the prenatal component of variance represents one half the additive genetic variance in body weight plus fractions of the dominance and epistatic variance as well as the effects of intrauterine environment. However, for later weights they reported results that corroborate the findings of the present experiment.

Except for birth weight, postnatal influence was statistically highly significant ($P < 0.01$) for every stage studied (Table 1). The postnatal component contains the variances due to maternal influences. Presumbly this would be mainly through lactation (Butler and Metrakos 1950). However, this component also would contain any common environment or cage effects (Hafez 1963; Rosenberg et al. 1970). The postnatal component of variance for birth weight was a small negative value and it was assumed to be zero. The expectation of this component for birth weight is zero, since postnatal influences have not been experienced at this point by the young mice. This supports the previous reports (Cox et al. 1959; Young et al. 1965; El-Oksh et al. 1967; Nagai 1971; Rut-

Table 1. Analysis of variance for individual weights at birth (W_0), 7 days (W_7), 14 days (W_{14}), 21 days (W_{21}) and 42 days (W_{42})

Source of variation	d.f.	W_0	W_7	W_{14}	W_{21}	W_{42}
Mean Squares						
Prenatal	76	0.0475^{++}	0.4098^{++}	0.5094^{++}	1.5347^{++}	4.8420^{++}
Postnatal	76[a]	0.0083	1.4887^{++}	2.4817^{++}	4.8185^{++}	4.8539^{++}
Prenatal × Postnatal	152[b]	0.0095	0.0833	0.1579	0.6233	2.2740
within	342[c]	0.0109	0.0682	0.1331	0.5093	2.2906
Components of variance						
Prenatal	(σ_a^2)	0.0063	0.0544	0.0586	0.1519	0.4280
Postnatal	(σ_p^2)	-0.0002	0.2342	0.3873	0.6992	0.4300
Prenatal × Postnatal	(σ_{ap}^2)	-0.0007	0.0075	0.0124	0.0510	-0.0083
within	(σ_e^2)	0.0109	0.0682	0.1331	0.5093	2.2906
Components of variance as percent of total[d]						
Prenatal	(σ_a^2)	37	15	10	11	13
Postnatal	(σ_p^2)	0	64	65	49	14
Prenatal × Postnatal	(σ_{ap}^2)	0	2	2	4	0
within	(σ_e^2)	63	19	23	36	73

[a] 66 for W_7, 54 for W_{14} and W_{21}, 24 for W_{42}

[b] 132 for W_7, 108 for W_{14} and W_{21}, 48 for W_{42}

[c] 297 for W_7, 243 for W_{14} and W_{21}, 108 for W_{42}

[d] Negative estimates of these components assumed as zero

++ Statistically significant ($P < .01$)

lege et al. 1972). The immediate and large influence of the postnatal environment is shown by the results for the weight at 7-, 14- and 21-days, where postnatal influences account for 64%, 65% and 49% of the total variance, respectively. These results indicate the importance of the postnatal maternal performance of the dam (milk producing ability plus any maternal ability associated with behaviour) in determining the growth of the young during the suckling period. Furthermore, the results indicate also (as expected) that the maximum influence of the postnatal environment was at 14 days of age. Jara-Almonte and White (1972) determined the lactation curve in laboratory mice by utilizing the difference in body weight of a litter before and after a 1.5 hour nursing period to obtain milk weights. The lactation curve reached a maximum between days 13 and 14 post partum. On the other hand, the young mice begin to consume solid food at around 14 days of age as soon as their eyes open. After this time the differences in genic values for growth would be expected to exert an influence on the animals growth response. However, the variance in the weight at 21 days is still largely influenced by the postnatal maternal environment (Table 1). This suggests that growth in mice until about 21 days of age is influenced more by postnatal maternal differences than by direct genetic differences. At 42 days of age, the postnatal component represents only 14% of the variance in individual weights. However, this indicates that the postnatal maternal influence of the nurse was nearly as important a source of variability in the weights of the young as were the hereditary and uterine factors which cause members of a litter to be more alike than individuals from unrelated litters (prenatal), until sexual maturity. The present results agree fairly well with those in the literature. Cox et al. (1959), Young et al. (1965) and El-Oksh et al. (1967) reported that postnatal effects account for over 60% of the total variance in

Table 2. Analysis of variance for individual weight gains from birth to 7 days ($W_7 - W_0$), from 7 to 14 days ($W_{14} - W_7$), from 14 to 21 days ($W_{21} - W_{14}$) and from 21 to 42 days ($W_{42} - W_{21}$)

Source of variation		d.f.	$W_7 - W_0$	$W_{14} - W_7$	$W_{21} - W_{14}$	$W_{42} - W_{21}$
Mean Squares						
Prenatal		66	0.4152^{++}	0.0929^{++}	0.5354^{++}	1.2777^{++}
Postnatal		66[a]	1.5058^{++}	0.7176^{++}	1.2668^{++}	0.6160^{++}
Prenatal × Postnatal		132[b]	0.0675	0.0526	0.3562^{+}	0.3893^{+}
within		297[c]	0.0646	0.0491	0.2570	0.2386
Components of variance						
Prenatal	(σ_a^2)		0.0580	0.0067	0.0299	0.1481
Postnatal	(σ_p^2)		0.2397	0.1108	0.1518	0.0378
Prenatal × Postnatal	(σ_{ap}^2)		0.0014	0.0017	0.0496	0.0754
within	(σ_e^2)		0.0646	0.0491	0.2570	0.2386
Components of variance as percent of total						
Prenatal	(σ_a^2)		16	4	6	30
Postnatal	(σ_p^2)		66	66	31	7
Prenatal × Postnatal	(σ_{ap}^2)		0,4	1	10	15
within	(σ_e^2)		17	29	53	48

[a] 54 for $W_{14} - W_7$ and $W_{21} - W_{14}$, 24 for $W_{42} - W_{21}$
[b] 108 for $W_{14} - W_7$ and $W_{21} - W_{14}$, 48 for $W_{42} - W_{21}$
[c] 243 for $W_{14} - W_7$ and $W_{21} - W_{14}$, 108 for $W_{42} - W_{21}$

+ statistically significant ($P < .05$)
++ statistically significant ($P < .01$)

7-, 14- and 21-day weight, while at 42 days of age this influence has declined by approximately 50%. Rutledge et al. (1972) indicate that the percent variance due to postnatal nurses had a maximum at 12 days, accounting for 68% of the variance in individual weights at this age. Thereafter, a decline was observed, yet significant postnatal maternal effects were present to day 49.

None of the prenatal by postnatal interactions was statistically significant (Table 1). The prenatal by postnatal interaction could arise through incompatibilities between the genotype of the mouse and the nutritional (milk) or cage environment provided by the nurse. The interaction component was positive (except for birth- and 42-day weight), but generally accounted for less than 4% of the variance in individual weights at different ages. These results suggest that the effect of transferring young from prenatal environments of one mother to postnatal environments of another mother is unimportant. The finding supports the previous reports (Cox et al. 1959; Young et al. 1965; El-Oksh et al. 1967; Nagai et al. 1971; Nagai 1971; Rutledge et al. 1972).

The error component of variance which also contains the remaining genotypic variance in weight and the random environmental influences, represented 63%, 19%, 23%, 36% and 73% of the total variance in the various body weights examined (Table 1).

Weight Gains

Estimates of mean squares and variance components derived from analysis of variance of weight gains examined are shown in Table 2. The components of variance expressed as a percentage of the total variance are also given. The prenatal component of variance represented a highly significant ($P < 0.01$). 16%,

4%, 6% and 30% of the total variance in gain during the period from birth to 7 days, 7 to 14 days, 14 to 21 days and 21 to 42 days, respectively. The maximum influence of the prenatal environment was thus during the postweaning gain period (21 to 42 days). This indicates that individual genetic factors influencing growth become relatively more important after weaning. In contrast, Young et al. (1965), El-Oks et al. (1967) and Rutledge et al. (1972) found that prenatal influences accounted for only 13%, 2% and 6%, respectively, of the total variance in gain from 21 to 42 days. The percent variance due to prenatal influences obtained in gain from birth to 7 days (Table 2) suggest that either the direct genetic effect and/or a carryover intrauterine effect of the prenatal dam may have real influence upon gain made immediately subsequent to birth. This result is in agreement with that of El-Oksh et al. (1967). They reported that prenatal influences accounted for 24% of the total variation in gain during the first week of age. In case of weight gain from 7 to 14 days and from 14 to 21 days, the influence of the prenatal effects clearly decreased (Table 2). This may reflect the fact that prenatal influences have less effect upon gains made during periods mostly influenced by the milk supply provided by the nurse. These results are in partial agreement with those of El-Oksh et al. (1967) who reported that prenatal effects accounted for 22% and 6% of the variance in gain during the same two periods, respecitvely.

A highly significant ($P < 0.01$) postnatal influence was observed in all gain periods studied (Table 2). Postnatal maternal influences accounted for 66% of the total variance in the first and second week's growth, respectively, then began a steady decline during the third week (31%) and finally were responsible for only 7% of the variance in gain from 21 to 42 days of age (Table 2). These figures are similar to those of 58%, 60%, 44% and 11% reported by El-Oksh et al. (1967) in the same gain periods, respectively. In general, the data of Cox et al. (1959), Young et al. (1965) and Rutledge et al. (1972) showed similar trends. In the case of preweaning gain, the present results suggest that the postnatal effect of the nurse has an important influence on growth of the young from birth to 14 days of age. This period is largely characterized by the lactational performance of the dam (Jara-Almonte and White 1972). Apparently the individual weight gain from 7 to 14 days is a better measure of milk production than the individual 14-day weight. Postnatal influences during this period of growth were more important than prenatal influences (66% vs. 4%), while in individual 14-day weight the percent variance was (65% vs. 10%) for postnatal and prenatal influences, respectively. Similar results were reported by Nagai (1971). In contrast, El-Oksh et al. (1967) reported that the absolute 14-day weight could be more sensitive to measure differences in milk production than the individual weight gain from 7 to 14 days of age.

The prenatal by postnatal interactions were not significant ($P > 0.05$) during the first two gain periods (birth to 7 days and 7 to 14 days), but were significant ($P < 0.05$) during the third and fourth periods (14 to 21 days and 21 to 42 days), Table 2. During the first two gain periods the interaction between prenatal and postnatal factors was apparently unimportant, as the component of variance accounted for less than 1% of the total variance in weight gains. The finding supports the previous reports (Young et al. 1965; El-Oksh et al. 1967; Rutledge et al. 1972). The interaction component of variance, on the other hand, accounted for 10% and 15% of the total variance in weight gain from 14 to 21 days and from 21 to 42 days of age, respectively (Table 2). These figures are in close agreement with those reported by El-Oksh et al. (1967), but are larger than those reported by Young et al. (1965) and Rutledge et al. (1972).

However, the present results indicate that genotype-environment interaction does not become important until late in the growing period when the genetic differences in the growing mice become more important and the postnatal influences of the nurse ceased to act.

The error component of variance represented 17%, 29%, 53% and 48% of the total variance during the four gain periods, respectively (Table 2).

Tail Lengths

Table 3 shows the mean squares, components of variance and the percentages they represent of the total variance in tail length at 21 and 42 days of age. This trait was included because even though it is genetical-

Table 3. Analysis of variance for tail length measured at 21 days (T_{21}) and 42 days (T_{42})

Source of variation		d.f.	T_{21}	T_{42}
Mean Squares				
Prenatal		54	0.1349^{++}	0.1784^{++}
Postnatal		54[a]	0.7767^{++}	0.3789^{++}
Prenatal × Postnatal		108[b]	0.0622	0.1413^{+}
within		243[c]	0.0657	0.0924
Components of variance				
Prenatal	(σ_a^2)		0.0121	0.0062
Postnatal	(σ_p^2)		0.1191	0.0396
Prenatal × Postnatal	(σ_{ap}^2)		-0.0017	0.0244
within	(σ_e^2)		0.0657	0.0924
Components of variance as percent of total[d]				
Prenatal	(σ_a^2)		6	4
Postnatal	(σ_p^2)		60	24
Prenatal × Postnatal	(σ_{ap}^2)		0	15
within	(σ_e^2)		34	57

[a] 24 for T_{42}
[b] 48 for T_{42}
[c] 108 for T_{42}
[d] Negative estimate for this component assumed as zero

\+ Statistically significant ($P < .05$)
++ Statistically significant ($P < .01$)

ly correlated ($r = 0.59$) with body weight (Falconer 1954), it may be related to skeletal size (Grüneberg 1957). The prenatal and postnatal components of variance accounted for 6% and 60% of the total variance in 21-day tail length, respectively, while a small negative value, assumed to be zero, was obtained for the interaction component. In the case of tail length at 42 days of age, the prenatal, postnatal and interaction components of variance accounted for 4%, 24% and 15% of the total variance, respectively (Table 3). The literature, except the study of Rutledge et al. (1972) seems devoid of any information concerning the prenatal and postnatal influences on tail length at different ages. Rutledge et al. (1972) reported slightly higher figures of 12% and 29% for the percent of variance due to prenatal and postnatal influences, respectively, in tail length at 42 days of age. The ratio of postnatal to prenatal components of variance allows an assessement of the relative importance of the two sources of variance. This ratio was 9.8 and 6.8 for 21- and 42-day tail length, respectively. Furthermore, the two ratios were larger for tail length than for body weight at the same age, where at 21 days of age the ratio was 9.8 vs. 4.6 and at 42 days of age was 6.4 vs. 1.0 for tail length and body weight, respectively. These results suggest that the maternal influences on traits may differ even when both traits are measured at the same age. The data of Rutledge et al. (1972) showed similar trends.

Literature

Bateman, N.: The measurement of milk production of mice through preweaning growth of suckling young. Phys. Zool. 27, 163-173 (1954)

Butler, L.; Metrakos, J.D.: A study of size inheritance in the house mouse. I. The effect of milk source. Can. J. Res. 28 D, 16-34 (1950)

Cox, D.F.; Legates, J.E.; Cockerham, C.C.: Maternal influence on body weight. J. Animal Sci. 18, 519-527 (1959)
Cox, D.F.; Willham, R.L.: Systematic fostering experiments in swine. J. Animal Sci. 21, 366-368 (1962)
El-Oksh, H.A.; Sutherland, T.M.; Williams, J.S.: Prenatal and postnatal maternal influence on growth in mice. Genetics 57, 79-94 (1967)
Falconer, D.S.: Selection for large and small size in mice. J. Genetics 51, 470-501 (1953)
Falconer, D.S.: Validity of the theory of genetic correlation. An experimental test with mice. J. Heredity 45, 22-44 (1954)
Grüneberg, H.: Genetical studies on the skeleton of the mouse. XIX. Vestigial-tail. J. Genetics 55, 181-194 (1957)
Hafez, E.S.E.: Symposium on growth; physio-genetics of prenatal and postnatal growth. J. Animal Sci. 22, 779-791 (1963)
Jara-Almonte, M.; White, J.M.: Milk production in laboratory mice. J. Dairy Sci. 55, 1502-1505 (1972)
La Salle, T.J.; White, J.M.: Characterization of reponse to selection for growth and maternal ability in laboratory mice. J. Animal Sci. 40, 48-50 (1975)
Legates, J.E.: The role of maternal effects in animal breeding: IV. Maternal effects in laboratory species. J. Animal Sci. 35, 1294-1302 (1972)
Nagai, J.: Preweaning weight as a measure of milk production in mice. Can. J. Genet. Cytol. 13 354-361 (1971)
Nagai, J.; Hickman, C.G.; Barr, G.R.: Selection index based on the nursing ability of the mother and the mature weight of the offspring in mice. J. Animal Sci. 40, 590-597 (1975)
Nagai, J.; Lee, A.J.; Hickman, C.G.: Preweaning growth of inbred, F_1 hybrid, and random-bred mice as a measure of mother's lactation. Can. J. Genet. Cytol. 13, 20-28 (1971)
Rosenberg, K.M.; Denenberg, V.H.; Zarrow, M.X.: Mice *(Mus musculus)* reared with rat aunts. The role of rat-mouse contact in mediating behavioural and physiological changes in the mouse. Animal Behav. 18, 138-143 (1970)
Rutledge, J.J.; Robison, O.W.; Eisen, E.J.; Legates, J.E.: Dynamics of genetic and maternal effects in mice. J. Animal Sci. 35, 911-918 (1972)
Young, C.W.; Legates, J.E.; Farthing, B.R.: Prenatal and postnatal influences on growth, prolificacy and maternal performance in mice. Genetics 52, 553-561 (1965)

Received July 26, 1977
Communicated by R. Hagemann

Prof. Dr. H. Brandsch
Dr. A.E.H. Kadry
Sektion Tierproduktion und
Veterinärmedizin
FG Haustiergenetik und Tierzüchtung
Karl-Marx-Universität
Fichtestraße 28
DDR-703 Leipzig
(German Democratic Republic)