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Catch-up growth malnutrition
growth velocity weaning

Catch-up Growth in Female Rats after Growth Retardation during the Suckling Period: Comparison with Males

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Extract

On the day of birth, the pups from several dams were pooled and reallocated so that some of the dams had 8 pups while others had 16. The pups were weaned at 21 days and placed 2 to a cage with unlimited food and water. The pups were weighed and measured on *days 3, 7, 14, 21, 28, 35, 49, 63, 77, 91, 105, 119,* and *228* and whole body radiographs were also taken, which enabled bone lengths to be measured and an assessment of skeletal maturity to be made. The experiment was continued until skeletal maturity reached 95% of the adult value in both groups. Data for females are reported and compared with those for males.

At weaning the undernourished females were only 63% ($P < 0.001$) of the weight of the normal females. After weaning, and hence during rehabilitation, the percentage difference between the groups progressively diminished; the undernourished were 67% ($P < 0.001$) of the normal group at 28 days, 72% ($P < 0.001$) at 35 days, 87% ($P < 0.01$) at 49 days, 93% at 91 days, and 95% (difference not significant) on completion of the experiment at 228 days. The total weight gain from 21 to 228 days was similar in both groups. The weight difference (15 g) was significant at 21 days when it represented a weight difference of 38% but the same weight difference (14 g) was not significant at 228 days when it represented a difference of only 5%.

In nose-rump length the undernourished were 84% of the normal rats at weaning. At 28 days they were 83% ($P < 0.001$), their velocity in length having nearly equalled that of the normals. From 28 days until 100 days their velocity exceeded that of the normals, so that by 35 days they were 91% ($P < 0.001$) of the length of the normals, by 49 days 95% ($P < 0.001$), by 63 days 99%, and by 90 days 100%. The catch-up was rapid and complete.

At weaning the tail length was 85% ($P < 0.001$) of the normals and at 28 days 82%. The catch-up in velocity was delayed until the 28–35-day period. The velocity exceeded that of the normal rats from 35 days on, and the undernourished caught up to 89% ($P < 0.001$) of the normals at 49 days and 95% ($P < 0.01$) at 90 days. At 228 days, however, catch-up was not quite complete, the undernourished being 96% of the normal, a difference which was just statistically significant ($P < 0.05$).

At 21 days the undernourished were about 1.5 days behind ($P < 0.001$) in skeletal maturity and at 35 days still further behind. After this the undernourished steadily caught up. At weaning the undernourished were slightly lower in weight and lengths for bone maturity, which indicated a greater effect on body measurements than on bone maturation. As in the males the two groups became equal for bone maturity at

a score which corresponded to about 28 days in normals and 35 days in undernourished. Thereafter there was little consistent difference in nose-rump length, but the tail length and weight in normal rats remained a little greater at given maturity score.

The effects of undernutrition in the females are qualitatively very similar to those in males, even in details of the growth curves. Quantitatively, the females, as expected, showed still greater capacity to catch up than males. At 35 days there is practically no difference in percentages between the sexes and thereafter in lengths and bone maturity the differences are very small. In weight, however, the undernourished males fare less well than the undernourished females. The difference is due to the greater increase of weight of the normal males from 105 days to 228 days. The sex differences clearly result from a lower mature weight for length in females and underline our previous conclusion that the lack of complete catch-up in weight under these experimental conditions results not from a skeletal deficit, but from a deficit in soft tissue.

Speculation

Female rats show a response to undernutrition during the suckling period similar to male rats, and a more nearly complete catch-up or rehabilitation. This study demonstrates that this statement applies to body weight but not to length, and indicates a differential susceptibility of nonskeletal tissues in males and females.

Introduction

Practically all studies of catch-up growth in experimental animals have dealt solely with males. Females have been used to examine the effects of growth depression on reproductive function [5, 6, 12, 14], but for little else. The probable cause for this can be found in Widdowson and McCance's remark that the "difference between the weights of fast and slow-growing males was considerably greater than the difference between those of the females." Workers who examine the results of undernutrition on growth have understandably chosen the system which most clearly demonstrates some effect. In terms of growth, however, the different responses of the sexes to perturbations in the growth curves are of interest as they may reflect differences in canalization [11]. In mammals the female appears to be more resistant to many types of insult, and returns to normal more rapidly (literature in Reference 10, p. 127). Greulich [1] found that children on Guam in 1947 after their war-time hardships were small and retarded in skeletal maturity, but boys were more affected than girls. Girl survivors of the atomic bombing of Japan were less retarded in growth 5 years later than were boys [2] and the same occurred with the Marshall Islands children exposed to atomic fallout in 1954 [9]. Widdowson and McCance [13] found that girls in a German orphanage in the malnutrition period just after the 1939–1945 war were less affected in height and weight than boys; Suoninen [8] has reported the same in children with congenital heart disease. That the sex difference is also seen in rats is clear from Widdowson and McCance's remark above, and from the work of Sikov and Noonan [7], for example, who showed that radiation affected the growth of females less than that of males. In a previous paper [15] we have described the response of male rats to undernutrition after weaning; here we describe and compare the response of the female.

Materials and methods

The strain of animals and the conditions of the experiment have been described previously [15]. Litters of 8 sibs (normals) and 16 sibs, (undernourished) were formed at birth, weaning was at 21 days, and nose-rump and tail lengths, weight, and skeletal maturity were measured at 3, 7, 14, 21, 28, 35, 49, 63, 77, 91, 105, 119, and 228 days. In the 8-litter group 10 females were present at *days 3, 7, 14,* and *21,* on *days 28, 35, 42, 49, 63, 77, 91, 105, 119,* and *228,* 8 animals were examined. In the 16-litter group, 15 animals were present at each time point up to 21 days, there were 12 animals present between *day 28* and *49,* and 11 at all subsequent times. The end point of the experiment was fixed when 95% skeletal maturity was reached by both groups. Statistical methods were the same as those described previously [15].

Results

Body Weight [18]: Figure 1

On *day 21,* the undernourished females were only 63% ($P < 0.001$) of the weight of the normal females. After weaning and hence during rehabilitation, the percentage difference between the groups progressively diminished, the undernourished being 67% ($P < 0.001$) of the normals at 28 days, 72% ($P < 0.001$) at 35 days, 87% ($P < 0.01$) at 49 days, 93% at 81 days, and 95% (difference not significant) at the completion of the experiment at 228 days. The velocity of the rehabilitating females never exceeded the velocity of the normals. The total weight gain from 21 to 228 days was similar in the two groups. The weight difference (15.4 g) was significant at 21 days when it represented a difference of 38% of total body weight but virtually the same weight difference (14.4 g) was not significant at 228 days when it represented a difference of only 5%.

Nose-Rump Length [18]: Figure 2

At weaning the pups from large litters were 84% ($P < 0.001$) of the normals. At 28 days they were 83%

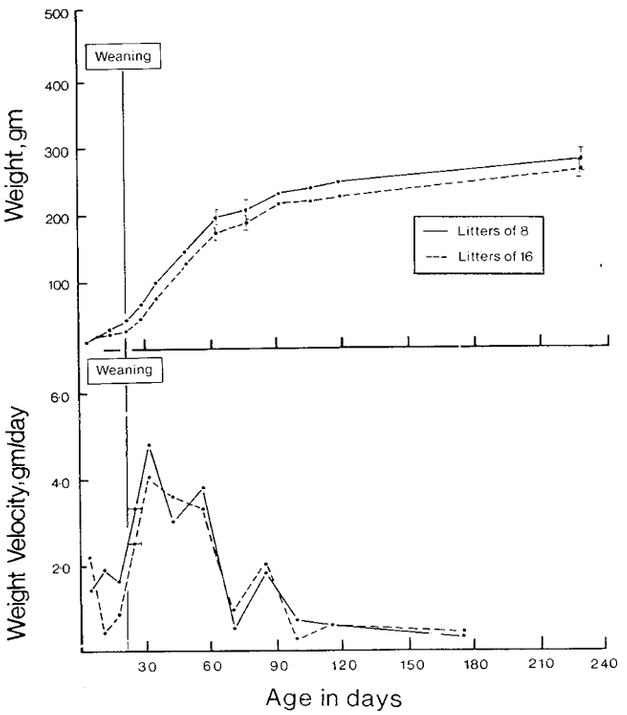

Fig. 1. Distance (*upper*) and velocity (*lower*) curves for the body weight of female rats reared in litters of 8 and 16 pups. The points on the velocity curve are plotted at the midpoint of the time period for which the velocity was calculated. The horizontal bars indicate the first velocity period after weaning.

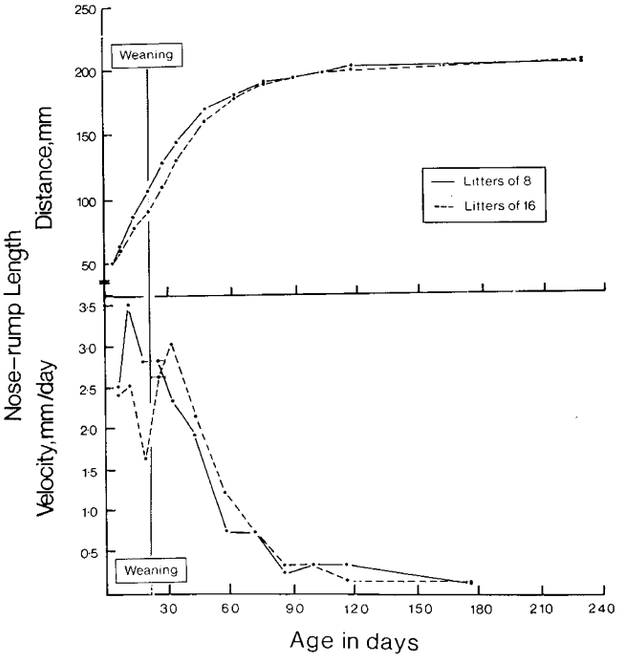

Fig. 2. Distance (*upper*) and velocity (*lower*) curves for the nose-rump length of female rats reared in litters of 8 and 16 pups. The points on the velocity curve are plotted at the midpoint of the time period for which the velocity was calculated. The horizontal bars indicate the first velocity period after weaning.

($P < 0.001$), their velocity in length having nearly equalled that of the normals. From 28 days until 100 days their velocity exceeded or equalled that of the normals, so that by 35 days they were 91% ($P < 0.001$) of the length of the normals, by 49 days 95% ($P < 0.001$), by 63 days 99%, and by 90 days 100%. The catch-up was rapid and complete.

Tail Length [18]: Figure 3

At weaning the tail length was 85% ($P < 0.001$) of that of the normals and at 28 days 82% ($P < 0.001$). The catch-up in velocity was delayed till the 28–35-day period, just as it was in the males. The velocity surpassed that of the normals, from 35 days on, and the undernourished caught up to 89% ($P < 0.001$) of the normal at 49 days and 95% ($P < 0.01$) at 90 days. At 228 days, however, catch-up was not quite complete, the undernourished being 96% of the normal, a difference which is just statistically significant ($P < 0.05$).

Skeletal Maturity [18]: Figure 4

By 14 days the score of the undernourished animals had fallen considerably behind ($P < 0.001$) and the difference increased until 35 days. At 21 days the un-

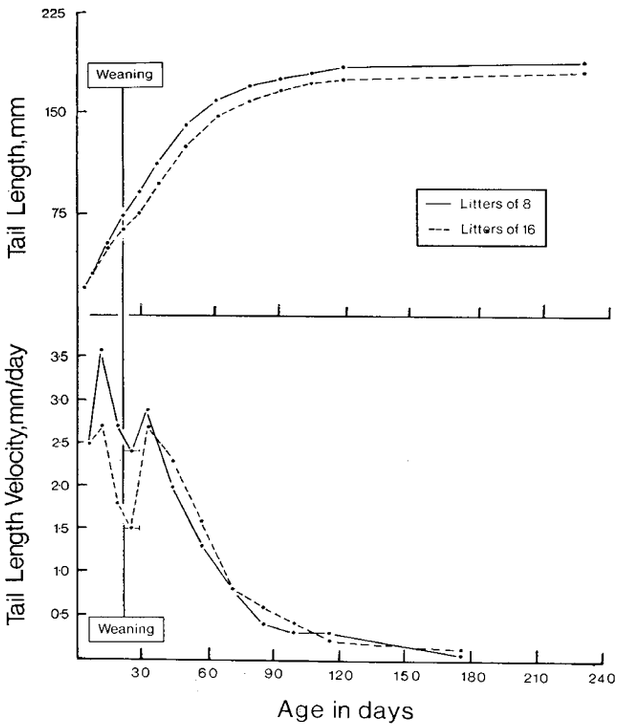

Fig. 3. Distance (*upper*) and velocity (*lower*) curves for the tail length of female rats reared in litters of 8 and 16 pups. The points on the velocity curve are plotted at the midpoint of the time period for which the velocity was calculated. The horizontal bars indicate the first velocity period after weaning.

dernourished were about 1.5 days behind and at 35 days still further behind. After this the undernourished steadily caught up. However, even at the end of the experiment the undernourished were still a little behind.

Weight and Lengths for Skeletal Maturity

Figure 5 shows weight, nose-rump length, and tail length plotted against skeletal maturity. At weaning the undernourished were slightly lower in weight and lengths for bone maturity, which indicates a greater effect on body measurements than on bone maturation. Exactly as in the males, the two groups became equal for bone maturity at a score of about 260, reached at 28 days in normals and 35 days in undernourished. Thereafter there was little consistent difference in nose-rump length, but the tail length and weight of the normals remained a little greater at given maturity score.

Discussion

The effects of undernutrition in the females are qualitatively very similar to those in males, even in details of the growth curves. Quantitatively, the females, as expected, showed still greater capacity to catch up than the males.

The mean percentages of normal for the undernourished groups of both sexes at successive ages are shown in Table I. At 35 days there was practically no difference in percentages between the sexes and thereafter in lengths and bone maturity the differences were very small. In weight, however, the undernourished males fared less well than the undernourished females. The difference was due to the greater increase of weight of the normal males from 105 days to 228 days, for at 105 days the undernourished were 91–92% of the well nourished in both sexes. The sex difference clearly results from a lower mature weight for length in females and underlines our previous conclusion that the lack of complete catch-up in males in weight under these experimental conditions results not from a skeletal deficit, but from a deficit in soft tissue, possibly fat.

The normal females of the present experiment were larger at 228 days than those reported in a previous study of Hughes and Tanner [3, 4]. The difference was

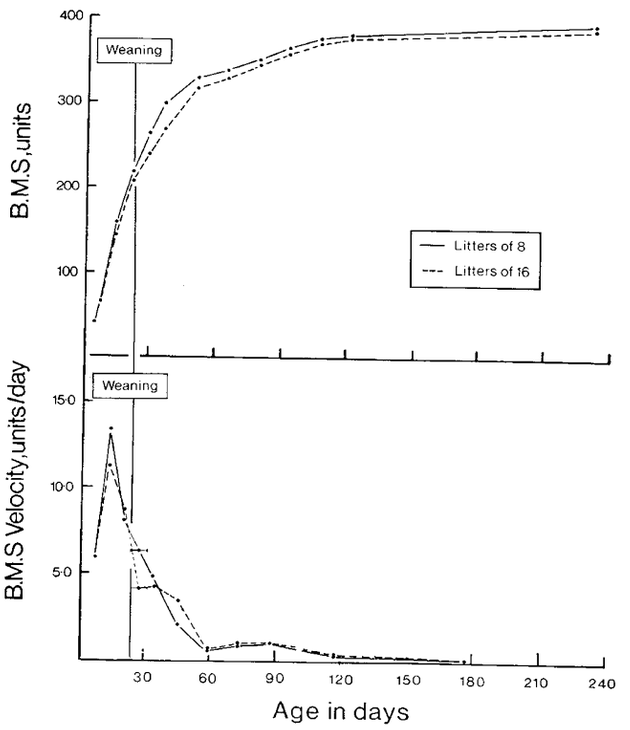

Fig. 4. Distance (*upper*) and velocity (*lower*) curves for the bone maturity score (*B.M.S.*) of female rats reared in litters of 8 and 16. The points on the velocity curve are plotted at the midpoint of the time period for which the velocity was calculated. The horizontal bars indicate the first velocity period after weaning.

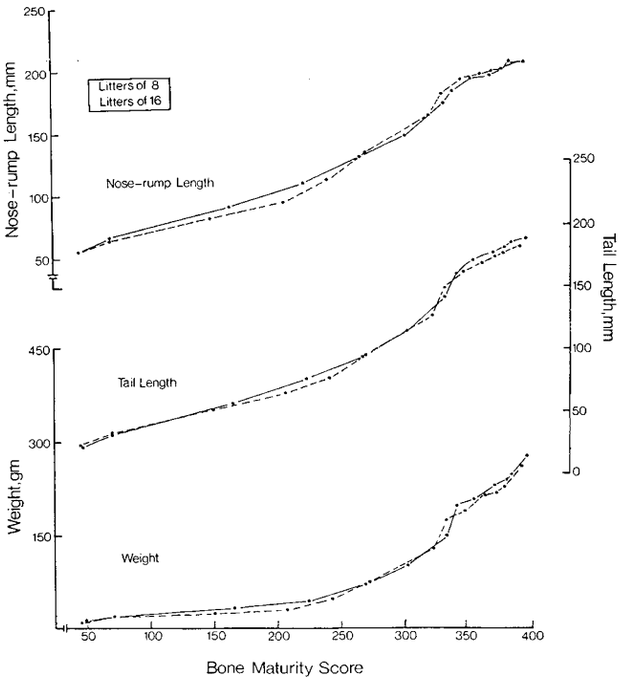

Fig. 5. Growth variables plotted against the bone maturity score for female rats reared in litters of 8 and 16 pups.

Table I. Mean of undernourished rats as percentage of mean of normals, males and females

Day	Weight		Nose-rump length		Tail length		Skeletal maturity	
	M	F	M	F	M	F	M	F
21	60	63	87	84	87	85	96	95
28	65	67	85	86	80	82	91	90
35	72	72	90	91	83	84	89	90
49	83	87	95	95	88	89	95	97
91	91	93	99	100	94	95	99	98
105	92	91	99	100	96	96	99	98
228	88	95	98	100	97	96	100	99

greater in weight (females in previous study 83% of those in present study) than in nose-rump length (98%): tail length was intermediate (94%). Similar results were obtained in the males. Inasmuch as the rats studied earlier were not weaned till 35 days, they were probably less well nourished from 21–35 days than the present ones, besides being reared during that period in more crowded conditions. This comparison therefore leads to conclusions similar to those in the present experiment.

If we are correct in thinking that the ultimate deficit in weight shown by the 16-sib males is due chiefly to permanent underdevelopment of their adipose organs [15], then the sex differences may be supposed to come about because the adipose organ of females is less easily affected during the suckling period. This would constitute yet another example of the greater resistance of the female to insult.

Summary

Female rats have been undernourished from birth to weaning by being placed in litters of 16 pups, compared with normal litters of 8 pups and then rehabilitated on unlimited food. Body weight, nose-rump and tail length, and bone maturity have been followed longitudinally until bone maturity was 95% complete and growth velocity practically zero.

The difference between normal and undernourished groups became nonsignificant in weight at 77 days (*i.e.* after 56 days rehabilitation) and in nose-rump length at 63 days; however, in tail length, the difference remained significant ($P < 0.05$) at 228 days, the end of the experiment, when the undernourished were 96% of the normal.

Comparison with similarly treated male animals showed that the females caught up somewhat more rapidly. However, the sexes differed significantly only in respect of weight deficit at 228 days, when males were 88% of the normals whereas the females were 95%. The sex differences in catch-up ability therefore relates to soft tissue only and not to the skeleton.

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18. Tables showing means, SD, *P* values, and numbers of animals for both the distance and velocity measurements of all variables may be obtained on request from the authors.
19. Requests for reprints should be addressed to: J. P. G. WILLIAMS, Ph.D., Department of Growth and Development, Institute of Child Health, University of London, 30 Guilford St., London W.C.1N 1EH, England.
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