Thus, the results of this research indicate that: (1) thalidomide interferes with the formation of endosteal bone induced by means of follicular hormone in the pigeon; (2) its action is manifested not by continuous slackening in the building of the trabeculae, but rather by causing their absorption between the 10th and the 15th day of treatment; and finally that (3) the absorption is not due to an increase in the number of osteoclasts in the same period of time.

Riassunto. Ricerche condotte sulla ossificazione endosteale indotta con ormone follicolare in piccioni trattati con talidomide hanno messo in evidenza che la talidomide interferisce con l'azione ormonale; la talidomide non inibisce la formazione delle trabecole ossee, ma provoca un notevole riassorbimento delle trabecole stesse tra il 10° e il 15° giorno di trattamento; tale riassorbimento non è imputabile ad un aumento del numero di osteoclasti nel periodo corrispondente.

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Development of Hyperphagia in Male Rats Following Placement of Ventromedial Hypothalamic Lesions at Four Different Ages[1]

A previous study[2] has shown that following ventromedial hypothalamic lesions, adult female rats showed a greater absolute food intake than did weanling animals. Relative to body weight, however, weanling and older rats ate similar amounts from the first post-operative week on. Rats lesioned during early and late adolescence showed similar food intake patterns throughout the experiment, regardless of whether food intake was expressed in g/day relative to body weight or relative to KLEIBER's 'metabolic size'[3]. It was suggested that age at operation and sensitivity of hypothalamic neurons might account for these findings[2]. The present note reports on a similar study in *male* rats. Methods and experimental conditions were identical with those in the study in the female animals[2].

(a) *Food intake in g/day* (Figure 1). During the first post-operative week only the oldest rats with lesions (140 days) showed hyperphagia when compared with their controls as well as with the 3 younger groups of operated rats. From the second week on, the 2 younger groups of rats with lesions (26 days and 59 days, respectively) ate similar amounts as their respective controls but the 2 older groups of rats (75 and 140 days, respectively) showed hyperphagia until the fifth week; during the sixth post-operative week all lesioned rats had plateaued to control levels. Among the operated animals, the rats lesioned at 140 days of age showed the highest food intake; during the sixth week all lesioned rats ate similar amounts.

(b) *Food intake relative to body weight* (Figure 2). The only group of rats to show a higher food intake than their controls during the first week of the experiment were the 140-day-old rats; however, they plateaued as early as the third week. Compared with their controls, rats lesioned

[1] This investigation was supported by U.S.P.H.S. Grant No. HE 06975 of the National Heart Institute.

[2] L. L. BERNARDIS, Experientia *22*, 593 (1966).

[3] M. KLEIBER, Physiol. Rev. *27*, 511 (1947).

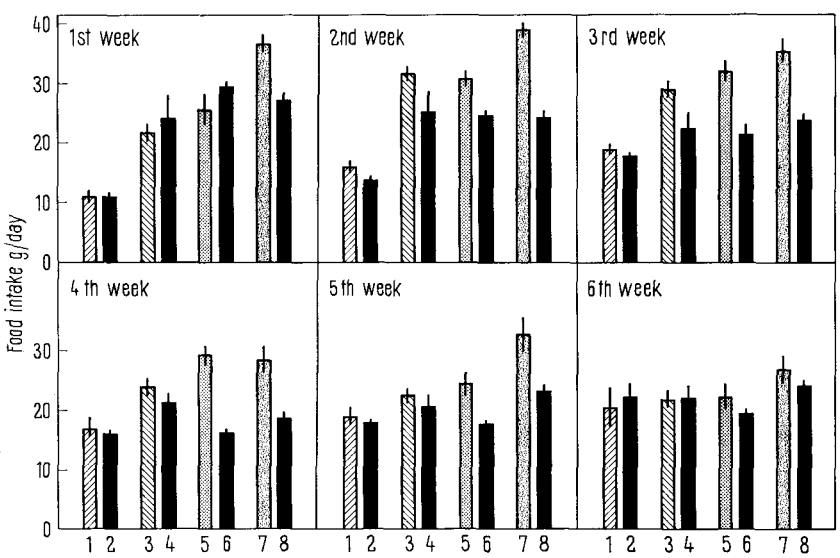

Fig. 1. Food intake in g/day of rats with hypothalamic lesions placed at the age of 26 days (group 1), 59 days (group 3), 75 days (group 5) and 140 days (group 7) and of their corresponding intact controls. Figures at bottom of diagram designate group number. Comparisons of means – First week: 7 vs 8, $p < 0.001$; second week: 1 vs 2, $p < 0.05$; 5 vs 6, $p < 0.05$; 7 vs 8, $p < 0.001$; third week: 3 vs 4, $p < 0.05$; 5 vs 6, $p < 0.01$; 7 vs 8, $p < 0.001$; fourth week: 5 vs 6, $p < 0.001$; 7 vs 8, $p < 0.01$; fifth week: 5 vs 6, $p < 0.02$; 7 vs 8, $p < 0.01$.

at 59 days ate similar amounts throughout the study but animals lesioned at 75 days ate more during the second, third and fourth week. Among the operated rats, the weanlings consumed more than the 3 older groups of animals throughout the experiment. Among the intact controls, the weanling rats showed the highest food intake also.

(c) *Food intake relative to 'metabolic size'* (Figure 3). Similar to the absolute (Figure 1) and the relative (Figure 2) food intake, only the oldest rats with lesions showed hyperphagia during the first week of the experiment. Similar to the absolute and relative food intake also, the 2 groups of older rats showed food intakes in the range of their respective controls. In contrast to the absolute and relative food intake; however, during the first week of the study the lesioned weanling rats ate as much as their controls.

(d) *Body weight* (Table). Terminal body weights of lesioned weanlings were similar to that of their controls, but the operated animals of the 3 older groups of rats showed significantly higher body weights than their controls.

Body weight at operation and 6 weeks thereafter at sacrifice of rats with ventromedial lesions placed at the age of 26 days (group 1), 59 days (group 3), 75 days (group 5) and 140 days (group 7) and of their respective controls (groups 2, 4, 6 and 8)

Group	Body weight at operation	Body weight at sacrifice
1	76 ± 2[a]	261 ± 18
2	76 ± 2	266 ± 10
3	238 ± 3	432 ± 12
4	236 ± 2	341 ± 7
5	324 ± 4	454 ± 11
6	328 ± 5	392 ± 8
7	469 ± 2	629 ± 13
8	471 ± 3	486 ± 11

[a] Mean ± S.E.M. Comparison between means: group 3 vs 4 $p < 0.001$; group 5 vs 6 $p < 0.01$; group 7 vs 8 $p < 0.001$.

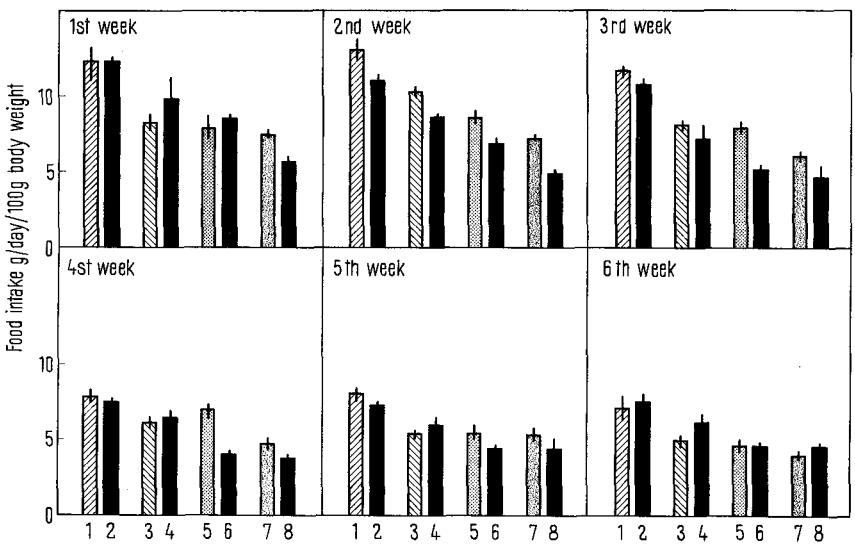

Fig. 2. Food intake in g/100 g body weight of rats with hypothalamic lesions and of their intact controls. For grouping see Figure 1. Comparisons of means – First week: 7 vs 8, $p < 0.001$; 1 vs 3, $p < 0.01$, vs 5, $p < 0.01$, vs 7, $p < 0.001$; second week: 5 vs 6, $p < 0.01$; 7 vs 8, $p < 0.001$; 1 vs 3, $p < 0.01$; 5 and 7, both $p < 0.001$; third week: 5 vs 6, 1 vs 3, 5 and 7, all $p < 0.001$; fourth week: 5 vs 6, $p < 0.001$; 7 vs 8, $p < 0.02$; 1 vs 3, $p < 0.02$; 1 vs 7, $p < 0.001$; fifth week: 1 vs 3, 5 and 7, all $p < 0.001$; sixth week: 1 vs 3, $p < 0.05$, vs 5, $p < 0.02$, vs 7, $p < 0.01$.

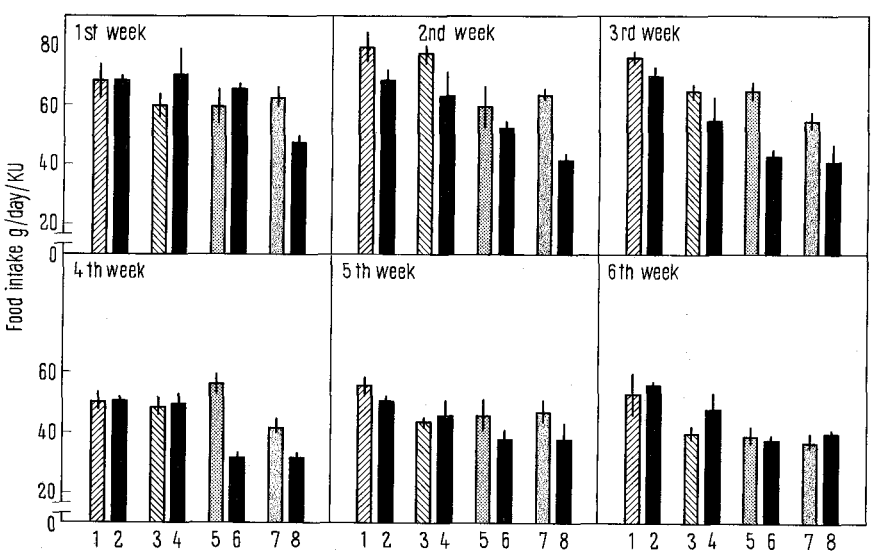

Fig. 3. Food intake in g per 'metabolic size' of rats with hypothalamic lesions and of their intact controls. For grouping see Figure 1. Comparisons between means – First week: 7 vs 8, $p < 0.001$; second week: 7 vs 8, $p < 0.001$; 1 vs 5, $p < 0.05$; 1 vs 7, $p < 0.01$; third week: 5 vs 6, $p < 0.001$; 7 vs 8, $p < 0.05$; 1 vs 3, $p < 0.01$, vs 5, $p < 0.02$, vs 7, $p < 0.001$; fourth week: 5 vs 6, $p < 0.001$; 7 vs 8, $p < 0.01$; fifth week: 1 vs 3, $p < 0.01$; sixth week: 1 vs 7, $p < 0.05$.

The present data indicate noteworthy sex differences with regard to food intake in rats lesioned at different ages. The unaffected absolute food intake during the first post-operative week in the male weanlings might be attributable to a decreased sensitivity of the lateral 'feeding center'[4] in the weanling male to the immediate effect of the lesion in the adjacent 'satiety center'[4]; the female weanlings[2] showed a depression of absolute food intake during this period. It is noteworthy, however, that already during this experimental period the oldest rats of both sexes showed gross hyperphagia.

It is of interest also that, while female rats lesioned at the age of 59 and 75 days, respectively, displayed hyperphagia throughout the experiment, their male counterparts began to plateau during the fifth week to control levels; in the same vein is the finding in the 140-day-old males which did not show the gross hyperphagia that was evident in the female rats of the same age when compared with their respective intact controls. This suggests that ventromedial lesions elicit greater hyperphagia in the adult female than in the adult male rat.

The data show also that, when food intake is expressed relative to body weight, weanling male rats consume more than corresponding females. The oldest rats with lesions, both male and female, however, show food intakes similar to that of their controls.

Expression of food intake relative to a seemingly more meaningful parameter, i.e. KLEIBER's 'metabolic size'[3] shows that there is little difference in whether food consumption is referred to this parameter or to body weight.

The data show that destruction of the ventromedial satiety neurons in the weanling male rat has no immediate effect on food intake and suggest a lesser sensitivity of the appropriate hypothalamic neurons[4] to the effect of the lesions. This is in contrast to the female rats. The data also reveal that, relative to body weight, the lesioned weanling rats ate more than older rats with lesions; female weanling rats ate similar amounts to older rats with lesions. Furthermore, male rats lesioned at later ages develop hyperphagia but this is not as pronounced as in correspondingly aged females. Male rats with lesions placed during adulthood plateau during the fifth week after the operation while corresponding females continue to show hyperphagia.

The sex difference in food intake may be related to a difference in body composition of males and females. That adipose tissue may play a role in the long-term regulation of food intake has been suggested by KENNEDY[5]. It is conceivable that the greater degree of adiposity in the lesioned female rats[2] than in the operated male animals did affect food intake[6].

Zusammenfassung. Im Gegensatz zu weiblichen Ratten zeigen männliche Tiere mit Läsionen des N. ventromedialis hypothalami im Alter von 26, 59, 75 und 140 Tagen kurz nach der Ablaktation keinen unmittelbaren Einfluss auf die Futteraufnahme, Erwachsene nie die in den gleichaltrigen weiblichen Ratten beobachtete Hyperphagie. Männliche Ratten erreichen das Kontrollniveau schon nach 5 Wochen, während die weiblichen Tiere noch ausgeprägte Hyperphagie zeigen.

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Department of Pathology, State University of New York at Buffalo (New York, USA), May 9, 1966.

[4] B. K. ANAND and J. R. BROBECK, Proc. Soc. exp. Biol. Med. *77*, 323 (1951).
[5] G. C. KENNEDY, Proc. R. Soc. B *140*, 578 (1953).
[6] The author is grateful to Dr. F. R. SKELTON for his help and support in this investigation.

Hemodynamic Studies in the Circle of Willis in the Rat

During the last 20 years a great deal of biochemical and related research has been conducted using rats rendered anoxic by ligation of both common carotid arteries for varying periods of time[1,2]. This study was undertaken to aid in assessing the functional significance of the vertebral arteries in the rat and thus to elucidate the biochemical results.

Methods. Adult male albino rats (Wistar strain) averaging 450 g in weight and anaesthetized with interperitoneal pentobarbital sodium (4 mg/100 g) were studied. Artificial respiration was used when necessary. The lingual arteries served as the recording sites to measure the back pressures of the circle of Willis as reported by AYALA and HIMWICH[3] for the dog. Occipital, pharyngeal and superior thyroidal arteries were ligated near their origin and the carotid sinus baroreceptors denervated with 10% formalin. The catheters used were intramedic polyethylene tubing of 3 sizes telescoped together: I.D. 0.034 in. · O.D. 0.060 in., I.D. 0.023 in. · O.D. 0.038 in. and I.D. 0.011 in. · O.D. 0.024 in. Actual recording was accomplished from the right and left lingual and systemic (femoral) sites simultaneously on a type 'R' Offner Dynograph through Model P23 Gd Statham pressure transducers. A definite sequential pattern of clamping was followed throughout the experiment. The pressures were allowed to equilibrate between each clamping (45 sec) and at the end of each series (3 min). On each experiment 2 clamping series were followed: The first consisted of the occlusion in sequence of the left common carotid artery (LCC), the right common carotid artery (RCC), the left vertebral artery (LV) and, the right vertebral artery (RV); the second series was a reversal and consisted of occlusion of the RV, LV, RCC and LCC. Readings were taken immediately after occlusion and again approximately 40 sec later; thus 16 readings in addition to control values were taken for each animal.

Results. The results presented for each series (Table), can be compared only with other data in that series. In series I when the total effect following bilateral occlusion of both carotid and vertebral systems is considered the systemic pressure (femoral) had a decline of 23.1% in mean pressure immediately after the RV occlusion, which was followed in 30 sec in all cases by a pronounced rise in pressure to a level approximately 33% higher than the

[1] L. JILEK, J. FISCHER, L. KRULICH, and S. TROJAN, in *Developing Brain, Progress in Brain Research* (Eds. W. A. HIMWICH and H. E. HIMWICH; Elsevier, Amsterdam, London, New York 1964), vol. 9, p. 113.
[2] R. G. SPECTOR, Br. J. exper. Path. *44*, 251 (1963).
[3] G. AYALA and W. A. HIMWICH, Am. J. Physiol. *201*, 443 (1961).