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Adipocyte Cellularity in the Desert Sand Rat (*Psammomys obesus*)[1] (38296)

R. PAUL ROBERTSON, B. R. BATCHELOR, P. R. JOHNSON, AND JUDITH S. STERN
(Introduced by E. L. Bierman)

University of Washington School of Medicine and Veterans Administration Hospital, Seattle, Washington 98108; and the Rockefeller University, New York, New York 10021

The desert sand rat (*Psammomys obesus*) is normally lean and subsists on vegetation in Middle Eastern deserts, but in the laboratory develops obesity, hyperinsulinemia, and in some instances, diabetes mellitus when fed *ad lib* chow (1, 2). It has been observed recently that obesity in this animal is associated with accelerated rates of endogenous triglyceride secretion (3). The sand rat thus represents a valuable investigative model of the interrelationships among obesity, diabetes mellitus, and lipemia. This model has the additional asset that obesity-induction takes place precisely as in man, *i.e.*, through spontaneous excessive caloric intake.

Obviously, to generalize from conclusions derived from studies of sand rats to obesity syndromes in other species, documentation that adipose tissue morphology in the sand rat is comparable to that in other species is required. Accordingly, in order to characterize morphologically the obese state in the sand rat, quantitative studies of adipose mass and of adipocyte size and number were performed.

Methods. Sand rats from a colony in Seattle, Washington, were transported by air to New York City. Male and female animals between 6 and 10 mo of age were used. Nutrition consisted of spinach, tap water, salt blocks, and Purina lab chow (56% carbohydrate, 5% fat). Obese animals were allowed unlimited access to Purina lab chow and lean animals were maintained on 30 g Purina lab chow daily. After their arrival in New York the animals were maintained on diets identical to those given in Seattle; one week later the experimental studies were performed. After an overnight fast, the animals were weighed at 8:00 AM and blood was drawn for plasma insulin and glucose determinations. Thereafter, the animals were stunned by a blow to the head, decapitated, and all dissectible fat was promptly removed from the epididymal, retroperitoneal, and subcutaneous fat depots. Total dissectible fat and carcass weights were recorded. Adipose cell size was determined by the method of Hirsch and Gallian (4) and adipose cell numbers and plasma levels of insulin and glucose were measured by methods previously reported (3, 5).

Results. The obese animals in both the male and female groups had significantly greater total body weight, total dissectible fat, mean adipocyte size and plasma insulin levels (Table I) compared to the lean animals. There were no significant differences in total adipocyte number; however, in the male animals there were significantly greater numbers of adipocytes ($P < 0.02$) in the obese group's subcutaneous (4.3819 ± 1.5217 vs $6.2684 \pm 0.9989 \times 10^6$) but significantly less ($P < 0.02$) in the obese group's epididymal (1.5956 ± 0.3411 vs $2.2265 \pm 0.4544 \times 10^6$) fat pads. None of the animals had fasting plasma glucose levels greater than 125 mg/100 cc. A variety of statistically significant linear correlations existed in the male group between total body weight, total dissectible fat, plasma insulin level, mean adipocyte

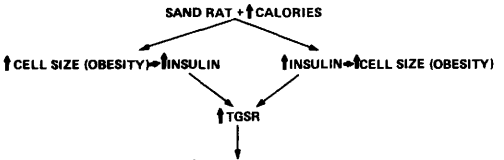

FIG. 1. Hypothetical events leading from increased caloric consumption to increased plasma triglyceride in sand rats.

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TABLE I. Comparison of Lean and Obese Sand Rats[a].

	Males		Females	
	Lean $N = 8$	Obese $N = 8$	Lean $N = 4$	Obese $N = 4$
Body weight (g).	164 ± 24	235 ±12***	150 ± 14	208 ±22**
Dissectible fat (g).	8.9 ± 5.4	25.6 ± 8.0***	12.5 ± 4.0	28.8 ± 2.6**
Mean adipocyte size (μg TG/cell).	0.3157 ± 0.1599	0.8007 ± 0.1598***	0.5752 ± 0.2731	0.9316 ± 0.1508**
Total adipocyte number × 10^6.	28.265 ± 6.090	31.606 ± 3.872	24.166 ± 5.872	32.041 ± 5.739
Plasma insulin (μunit/ml).	91 ± 67	726 ± 479***	213 ± 50	1498 ± 877

[a] All values expressed as mean ± SD. Statistical comparisons (* = $P < 0.05$, ** = $P < 0.01$, *** = $P < 0.001$) are between lean and obese animals of the same sex. There were no significant differences between male and females when comparing lean with lean and obese with obese animals.

size, and total adipocyte number, all of which are shown on Table II. Correlation analysis was not performed on the female group because of the small numbers of animals.

Discussion. These studies demonstrate that obesity-induction by high caloric feeding in male and female postadolescent sand rat is associated with increases in dissectible fat, adipocyte size and circulating insulin levels but no significant change in total adipocyte number. These cellularity characteristics are comparable to those found in other animals and in man (6–8), and, therefore, the sand rat appears to be an appropriate model for studying obesity. It is difficult to cross-compare adipocyte cellularity of sand rats with other animal species examined with regard to absolute values, but it appears that the adipocyte size in the lean sand rat is comparable to sizes noted in other lean animals, whereas the adipocyte number in lean sand rats appears to be 2–10 times as great (6). It seems unlikely, however, that this tendency toward a larger adipocyte number in lean sand rats is the explanation for the high basal insulin levels in lean sand rats observed previously (3) and again in this study since it was adipocyte size and not number which had a significant correlation with plasma insulin levels.

When one attempts to interrelate obesity, hyperinsulinemia and accelerated triglyceride secretion in the sand rat, at least two possibilities come to mind, as shown in the accompanying diagram. Increased caloric consumption may lead to increased insulin secretion and hyperinsulinemia, which in turn would both promote adipocyte storage of triglyceride (TG) by virtue of insulin's antilipolytic and lipogenic effects and also enhance endogenous triglyceride secretion (TGSR), as has been previously shown (3). Alternatively, increased caloric consumption might lead directly to increased adipocyte size which in turn would cause increased peripheral insulin resistance, compensatorily increased insulin secretion, hyperinsulinemia and eventually enhanced endogenous triglyceride secretion. Either sequence of events would account for the increased circulating levels of triglyceride associated with obesity in the sand rat (3).

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TABLE II. Correlations Between Various Measurements in Lean and Obese Male Sand Rats ($N = 16$).

	Correlation coefficient	P value
Body weight and dissectible fat	0.84	<0.001
Body weight and plasma insulin	0.68	<0.01
Body weight and mean adipocyte size	0.87	<0.001
Body weight and total adipocyte number	0.51	<0.05
Plasma insulin and dissectible fat	0.58	<0.02
Plasma insulin and mean adipocyte size	0.61	<0.02
Dissectible fat and total adipocyte number	0.61	<0.02

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