Hunger Drive During Starvation in Rats Enriched with Odd-Carbon Fatty Acids[1] (37443)

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When a diet containing triundecanoin as the major fat source is fed to weanling rats for 4–6 weeks, they show substantial enrichment of depot fat with undecanoate and higher fatty acids with odd-numbered carbons (1). Animals so enriched maintain significantly higher concentrations of liver glycogen and serum glucose during starvation than do controls previously fed a diet containing a conventional fat source (2, 3). This response appears to occur because the terminal 3-carbon residues arising from beta-oxidation of mobilized odd-carbon acids are glucogenic (4) and thereby counteract in part the marked decreases in liver glycogen and serum glucose ordinarily induced by prolonged fasting (5). In the nonfasted state, rats enriched with odd-carbon fatty acids do not differ significantly from controls in regard to concentrations of glycogen in liver and glucose in serum (2, 3).

Because reserves of nonprotein precursors of carbohydrate are appreciably expanded in rats enriched with odd-carbon fatty acids, this animal preparation seemed to provide a unique model to test whether the carbohydrate privation associated with starvation has an effect on drive for food separate from that of overall calorie depletion (6). Accordingly, we conducted experiments to compare strength of motivation to obtain food following a period of food deprivation in rats enriched with odd-carbon fatty acids and conventionally fed controls.

Methods and Results. Subjects were 42 female Charles River CDF strain rats purchased as 28-day-old weanlings and immediately placed on the test diets, on which they were initially maintained for 7 weeks. The diets, which were powdered, were nutritionally complete, with the following calorie distribution: 19% protein, 51% carbohydrate, and 30% fat. For half of the group, the fat component of the diet consisted of 30% corn oil and 70% triundecanoin, a synthetic odd-carbon triglyceride (Drew Chemical). For the remaining 21 animals, the fat component was composed entirely of corn oil.

All rats were fed and housed in individual cages with water always available. Weight gains over the 7-week period were similar for the two groups. In the eighth week, *ad libitum* food intake was recorded for seven days. Daily food intake averaged 10.4 g for the odd-carbon-enriched (OCE) rats and 10.5 g for the control animals. Mean body weight for the control animals was 171.1 g and for the OCE rats, 172.1 g. Subsequently, when the animals were periodically starved, they were always permitted to regain their predeprivation weight on their usual diet.

Behavioral Studies. In the ninth week, rats were trained to lever-press in standard operant conditioning chambers, equipped with a lever, house lights, water tube, and feeder mechanism for delivery of 45 mg food pellets made from either the control or experimental diet. Test chambers were housed inside sound attenuating boxes and electro-mechanical scheduling and recording equipment was located in an adjacent room. After the lever-press response was learned, each animal was given three 1-hr sessions of continuous rein-

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forcement (CRF) during which each lever-press was rewarded by a 45 mg food pellet. For the first and second sessions, animals were food-deprived for 24 hr before each session, and for the third session for 48 hr in order that major differences in blood sugar levels between OCE and control groups would be assured (2). After 48 hr of deprivation the mean number of responses per 5 min of CRF for the OCE group (11.3) was not significantly different from that of the controls (12.2).

Activity following 0 and 48-hr food deprivation also was recorded for both groups. Three standard 15-min tests were used (open field, photocell cage, and light-contingent bar-pressing) (7). No significant differences were found under either condition between OCE and control rats. *Ad libitum* feeding patterns were recorded daily for ten days on four animals from each group. There were no significant differences in meal size, meal number, or intermeal intervals between the two groups.

After their body weights had returned to normal, all animals were again deprived for 48 hr and tested once on a progressive ratio (two) schedule (8), which was chosen because it has been found to be particularly sensitive to differences in level of food motivation. On this schedule, the animal is required to make 2 presses for the first reward, 4 for the second, 6 for the third, and so on. The "breaking point" is reached when the rat fails to obtain a reinforcement in 20 min. The number of presses made to obtain the last reward was the score assigned to each animal. The mean number of presses made to obtain the final reinforcement was 40.6 for the OCE group and 67.4 for the control group (t (40) = 2.840, $p < 0.05$). The clear difference in distribution of breaking-point scores between the two groups of animals is shown in Fig. 1.

Metabolic Studies. After completion of the behavioral experiments, animals were given *ad libitum* access to their usual diets and permitted to regain their lost weight. Then, the concentrations of glycogen in liver and of glucose in plasma, and the fatty acid composition of perirenal fat were measured in all of the animals after a 48-hr fast. The animals were killed by decapitation and blood samples collected in heparinized tubes within a few seconds. Liver and perirenal fat samples were removed immediately thereafter. Wedges of liver were crushed directly in 30% KOH and fragments of perirenal fat were placed in chloroform–methanol (2:1). Plasma glucose was determined by means of an automated procedure based on the method of Hoffman (9), and liver glycogen was measured by the method of Good *et al.* (10). The fatty acid composition of lipid extracts of perirenal fat was measured by temperature-programmed gas–liquid chromatography.

Concentrations of undecanoate in perirenal fat from the OCE rats averaged 21.2%, with the range from 18.1 to 25.4. The average

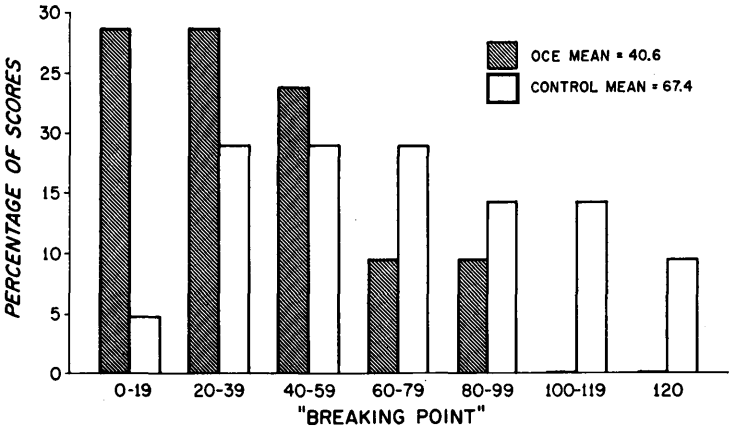

FIG. 1. Distribution of "breaking-point" scores on the Progressive Ratio (two) Schedule for odd-carbon-enriched (OCE) and control rats.

content of longer odd-numbered fatty acids ranging from C_{13} to C_{17} was 1.5%. Following 48 hr of starvation, liver glycogen concentrations in the control group were very low, averaging (± SD) 0.15 ± 0.10 g/100 g. Liver glycogen in the OCE group averaged 0.95 ± 0.36 g/100 g after 48 hr of deprivation ($p < 0.001$). Similarly, at 48 hr, plasma glucose concentrations averaged 95.8 ± 6.3 mg/100 ml in the control rats and 115.2 ± 7.6 mg/100 ml in the OCE animals ($p < 0.001$).

Discussion. The results of the progressive ratio study suggest that the OCE rats have a lower hunger drive after 48 hr of starvation than do the normally fed controls. Further tests of food-motivated behavior will be necessary to establish the generality of this finding.

Whether this reduced drive for food in the OCE rat is directly attributable to the unique ability of this animal preparation to resist carbohydrate depletion during starvation, or whether it results from some other associated metabolic phenomenon, is not yet clear. It should be emphasized that, in our study, the OCE rats were subjected to the same degree and duration of calorie deprivation as their normally fed controls; however, after 48 hr of starvation they maintained significantly higher concentrations of glucose in plasma and glycogen in liver. Another study (3) has shown that during starvation, OCE rats also exhibit higher serum levels of immunoreactive insulin and lower serum concentrations of free fatty acids than do comparably deprived controls. In addition, OCE dogs show significantly less ketonemia during starvation than do control animals (11). These observations indicate that, during starvation, OCE animals utilize a higher than usual proportion of carbohydrate to support their energy needs.

In the past it was virtually impossible to design chronic experiments that could dissociate physiologic responses to carbohydrate privation from those to overall calorie depletion. The OCE animal preparation permits an appreciable separation of these two variables. Our present results suggest that, during starvation, the available supply of carbohydrate has an effect on hunger drive distinct from that induced by overall calorie deprivation.

Summary. Rats with depot fat enriched with undecanoate maintain significantly higher concentrations of liver glycogen and plasma glucose during prolonged starvation than do conventionally fed controls. When food motivated behavior was tested by means of a progressive ratio schedule of reinforcement, the undecanoate-enriched rats exhibited a significantly lower drive for food after 48 hr of starvation than did their nonenriched controls.

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