Food-deprivation polydipsia in gerbils: Lack of adaptive value and termination with carbohydrate feeding

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The causation of water polydipsia which occurs during food deprivation in the gerbil was examined. Survival times during food deprivation were not decreased by preventing polydipsia, as would be expected if polydipsia were due to renal dysfunction. Feeding pure carbohydrates abolished polydipsia, without reversing weight loss. It was concluded that there was no evidence to demonstrate that polyuria is primary to polydipsia.

It is now well documented that totally or partially food-deprived gerbils develop polydipsia (Kutscher, 1969; Reynierse, Scavio, & Spanier, 1970) and polyuria (Kutscher, Stillman, & Weiss, 1968). Gerbils reach peak water intake on Days 4-7 of total food deprivation, and some individual animals consume in 1 day water equivalent to their body weights (Kutscher, 1969). The physiological correlates of food-deprivation polydipsia (FDP) in the gerbil have yet to be elucidated. It seems important at the outset to establish whether FDP is primary and the polyuria is a necessary physiological consequence of voluntary water loading or whether polyuria is primary and the FDP is a corrective response to water deficit.

Previous research has not clearly settled this problem. Kutscher et al (1968) showed that gerbils that were food deprived and polydipsic could still excrete hypertonic urine and sharply reduce urine output when challenged by water deprivation and salt injection. In other laboratory animals, polydipsia occurs as a consequence of renal dysfunction produced by sodium (Holmes & Cizek, 1951) or potassium deficit (Brokaw, 1952), two possible consequences of food deprivation, but FDP in the gerbil was not prevented or even attenuated by supplementary feeding of sodium (Kutscher et al, 1968) or potassium (Stillman, 1969) during deprivation. On the other hand, Milligan, Hotson, Ripley, and Tait (1969) reported that FDP in partially food-deprived gerbils was prevented when urea was added to the food ration in an amount equivalent to the protein nitrogen removed by the food-deprivation schedule. They reasoned that polyuria was probably primary and FDP secondary because the apparent protein deficiency during deprivation probably reduced blood urea levels to such a degree that renal concentrating mechanisms were impaired. Although this explanation is at variance with data of Kutscher et al (1968), it does seem reasonable in light of current knowledge of renal physiology (Crawford, Doyle, & Probst, 1959; Dicker, 1970, p. 58).

If FDP is due to primary polyuria caused by renal dysfunction and if that dysfunction is due to protein or urea deficiency, then the following experimental outcomes would be expected: (a) gerbils should survive

longer under total food deprivation if allowed to become polydipsic than if restricted to the level of water intake present during ad lib feeding, and (b) feeding of pure carbohydrates which cannot be directly converted into urea should not terminate the polydipsia. These experiments were done to test these two hypotheses.

EXPERIMENT I

Method

Subjects

Twenty-four male gerbils (*Meriones unguiculatus*), 200 days old, 57-100 g, were used as Ss in this experiment. Gerbils were obtained from Tumblebrook Farms, Brant Lake, New York.

Apparatus

During the experiment, gerbils were housed individually in standard cages of steel and hardware cloth (10 x 8 x 7 in.). Purina Laboratory Chow was fed in pellet form and tap water was given in inverted 100-ml graduated cylinders (graduated in 1-ml units) fitted with steel drinking spouts. Temperature was maintained at $71^{\circ} \pm 2^{\circ}$ F. Lights were on for 12 h/day.

Procedure

Gerbils were placed in cages and were given 7 days to adapt. Daily measures of body weight and food and water intake were made during 6 days of ad lib feeding. All gerbils were then subjected to terminal, total food deprivation. Animals were randomly divided into two groups of 12 each. One group, the nonpolydipsic group, received one daily ration of water equal to the mean group intake during ad lib feeding. The other group, the polydipsic group, was allowed continuous free access to water. Survival time was recorded in 1/3-day units for each animal.

Results

All animals survived at least 5 days of total food deprivation. As Fig. 1 shows, mean water intake for the polydipsic group increased progressively during the first 6 days of deprivation and a vigorous FDP occurred. The mean survival time of the polydipsic group was shorter (9.7 days), not longer, than that of the nonpolydipsic group (12.8 days). This difference was significant ($t =$

Fig. 1. Mean daily water intake of the polydipsic group in Experiment I. Numbers in parentheses indicate numbers of animals surviving.

2.22, $df = 22$, $p < .05$). Mean weight loss at death was 35.8% of predeprivation body weight for the polydipsic group and 43.4% for the nonpolydipsic group. This difference was also significant ($t = 2.26$, $df = 22$, $p < .05$). Thus, FDP seems to have no adaptive value. Indeed, it is somewhat maladaptive since animals allowed to become polydipsic during food deprivation die sooner after less weight loss than those not permitted to become polydipsic.

EXPERIMENT II

Method

Subjects

Twenty-eight gerbils, 14 male and 14 female, 200 days old, 48-88 g, were used as Ss in this experiment. Both sexes were used because Weiss (1969) found no differences in the incidence and degree of FDP shown by male and female gerbils over a broad age range. Eighteen of the animals had been used previously in two short experiments involving partial food deprivation, but they were allowed at least 30 days to recover.

Procedure

Gerbils were placed in cages and allowed 7 days to adapt. Water intakes were then measured daily during 6 days of ad lib feeding. Gerbils were subjected to 3 days of total food deprivation, followed by 1 day of refeeding. Water was freely available at all times. During refeeding, 15 Ss were given Purina Chow in mash form and 13 Ss were given a 50-50 mixture of sucrose and corn starch (mixed by weight) presented in glass foodcups. Animals were weighed at the beginning and end of the deprivation interval and after 1 day of refeeding.

Results

The effects of feeding Chow and the sucrose-starch mixture on the termination of FDP are shown in Fig. 2. Both groups developed vigorous polydipsia during the 3

days of food deprivation. Upon refeeding, the mean water intake for the Chow group (14.1 ml) was significantly less ($t = 3.82$, $df = 13$, $p < .01$) than that on the last deprivation day (25.8 ml), but was significantly higher ($t = 8.29$, $df = 13$, $p < .01$) than intake on the last ad lib day (7.1 ml). Mean weight gain for this group during 1 day of Chow feeding was 5.6 g, or 9.2% of predeprivation body weight, leaving a residual body-weight deficit of 9.7%.

For the sucrose-starch group, mean water intake during the refeeding day (2.6 ml) was significantly less ($t = 3.70$, $df = 11$, $p < .01$) than intake on the last ad lib feeding day (6.4 ml) and significantly less ($t = 3.74$, $df = 11$, $p < .01$) than intake on the last day of food deprivation (22.8 ml). Thus, carbohydrate feeding not only abolished FDP, but also depressed drinking below ad lib levels, even though body-weight deficits persisted. Mean body-weight deficit was 16.3% at the beginning of the refeeding day and 18.7% at the end. Nine out of the 13 gerbils in this group drank only 3 ml or less during the refeeding day. The failure of carbohydrate feeding to prevent weight loss may have been due to low intakes of this novel food. In spite of this, FDP was eliminated in every animal.

DISCUSSION

It is clear that the original hypotheses of the author concerning FDP were not confirmed. The fact that polydipsia confers no survival advantage to the gerbil during food deprivation suggests that the animal simply does not need the massive amounts of water which are consumed. This fits well with the findings of Kutschner et al (1968) suggesting that FDP probably is not due to

Fig. 2. Mean daily water intake for the two groups in Experiment II. One received Chow on the refeeding day and the other received the sucrose-starch mixture.

kidney dysfunction. Vigorous polydipsia without apparent water deficit is not unprecedented. In schedule-induced polydipsia in rats (Falk, 1969) and mice (Palfai, Kutscher, & Symons, 1971), certain schedules of food delivery result in vigorous polydipsia in the absence of apparent water need.

The mildly deleterious effects of FDP on survival time may be due to the additional metabolic energy required to warm the self-inflicted water loads to body temperature and to excrete the copious amounts of dilute urine (Kutscher et al. 1968). Therefore, this finding is possibly not as important as the failure to find extremely short survival times in the nonpolydipsic group. If FDP were secondary to polyuria, it might be expected that deaths would occur in the nonpolydipsic group soon after the second or third day of total food deprivation, since this is when FDP appeared in the polydipsic group. Unpublished observations by the author on the SWR inbred mouse strain, which develops nephrogenic diabetes insipidus with age, showed that death occurred within 24-48 h after the introduction of water restriction.

The method of terminal deprivation is an extreme procedure, but only the use of prolonged deprivation permits quantitative statements concerning the survival value of FDP. It should be pointed out, however, that FDP is not a symptom of morbidity, but can be produced and maintained for long periods of time on partial food-deprivation schedules (Kutscher, 1969), even when gerbils suffer only a 5% weight loss and are healthy and vigorous (unpublished observations).

Perhaps the data of Experiment II may provide another perspective for the study of FDP. The protein deficiency hypothesis suggested by Milligan and coworkers (1969) requires some qualification, as FDP can be immediately eliminated by carbohydrate feeding which should not directly restore normal levels of protein or nonprotein nitrogen. It is not clear, however, what the site of action of the carbohydrate is. There are also known interactions between carbohydrate ingestion and protein metabolism, although it is not clear how any of these relationships can abolish FDP. Glucose contributes carbon skeletons for the synthesis of nonessential amino acids and provides the substrate for compounds which serve a catalytic function in catabolic sequences (Cantarow & Schepartz, 1967, p. 394). Also during food deprivation, glucose ingestion provides a ready source of energy and thus has a "sparing" effect on body protein which otherwise would be utilized for energy (Cantarow & Schepartz, 1967, p. 550). In the above experiments, however, probably no protein synthesis occurred during carbohydrate feeding, as food-deprived gerbils are probably in a state of negative nitrogen balance, as is the case in fasting humans (Grande, 1964) and dogs (Rosenthal & Allison, 1951).

There seems to be no compelling evidence at this point that FDP is precipitated by a primary polyuria, but it should be noted that there are at least two

possible ways that sucrose intake might directly affect renal metabolism and function. First, Dicker (1970, p. 611) stated that all portions of the kidney tubules, with the exception of the proximal tubules, depend upon glycolysis for energy. Thus, carbohydrate feeding at the end of 3 days of food deprivation may provide a readily usable energy source to an animal which has probably exhausted the carbohydrate stores of the body. Secondly, the kidney, along with the liver and intestinal mucosa, is a site of very active protein metabolism (Cantarow & Schepartz, 1967, p. 550). Carbohydrate feeding could produce a "sparing" effect by slowing or stopping catabolism of renal protein.

The inhibition of drinking is not due to stomach filling. Inspection of the gastrointestinal system of gerbils following 1 day of refeeding on the sucrose-starch mixture disclosed that stomachs were virtually empty of contents and only small amounts of the carbohydrate mixture were found in the small intestine. Other explanations of the mechanism of carbohydrate depression of drinking and the abolition of FDP can only be speculative at this time. It is possible that the carbohydrate in some form, perhaps as glucose, directly affects critical brain structures, resulting in the suppression of drinking. Whatever the mechanism, the suppression of drinking has a short latency. For example, Animal No. 16 drank 80 ml of water on the third deprivation day (mean hourly intake = 3.2 ml), but on the refeeding day intake for the entire 24-h period was only 5 ml. It is unlikely that any of the low water intakes on the refeeding day were due to inanition, since body-weight losses at the beginning of the refeeding period in Experiment II were approximately half those at death in Experiment I. Furthermore, all animals appeared active and vigorous at the end of deprivation. Instead, these data suggest that the study of the causation of FDP in the gerbil should include a study of carbohydrate metabolism and its significance for body-water balance.

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