Brief Communication

Caloric Imbalance Induced by Failure of Food Intake to Compensate for Caloric Supply Provided by Diurnal or Nocturnal Drinking of Isotonic Glucose

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The phenomenon of paradoxical stimulation of food intake by duodenal infusion of larger loads of isotonic glucose resulting in a short-term caloric imbalance has now been well substantiated ([12], Rezek, et al., publication pending). Its expression was shown to be causally dependent on the prolonged and exaggerated release of insulin since any reduction or elimination of this endocrine response prevents the development of this phenomenon. The obvious question which remains to be answered is the duration for which the caloric imbalance will be tolerated following longer carbohydrate challenge than in the original experiment. The possibility of prolonged caloric imbalance would be of greater regulatory importance with significant implications for the normal maintenance of energy balance.

In the present experiment, diurnal or nocturnal carbohydrate loading was employed and the ability of food intake regulatory mechanism to compensate for this caloric supply was examined.

METHOD

To examine the earlier stated hypothesis, a simple but natural method has been used. Thus food intake was monitored following diurnal or nocturnal drinking of isotonic glucose or saccharin solutions. This was analysed for the absolute food and carbohydrate caloric intakes and compared with corresponding control values determined after drinking of tap water. The animals had free-access to food at all times regardless if they were drinking water, glucose or saccharin. The measurements of food and fluid intakes were performed between 9 a.m. and 3 p.m. (diurnal period) and between 3 p.m. and 9 a.m. (nocturnal period).

Fifteen rabbits in three groups of 5 animals each were exposed in counterbalanced manner to all three solutions (5 days at each solution) during the day or night period while provided with tap water during the alternate period.

Included in present report are also the results of additional testing of the mechanism pertaining to the mediation of the original phenomenon. This involved faster duodenal infusions of larger glucose loads (30 ml), duodenal infusions of iso-osmotic-iso-volumic solution of saccharin which has not been tested previously and a blockade of lipogenesis by pretreatment with Atromid S 9 100 mg/kg) prior to the duodenal infusions of larger glucose loads. For these additional experiments the animals were implanted with chronic duodenal and intraperitoneal cannulas according to the technique described previously [3].

RESULTS

The results of drinking experiments are graphically summarized in Fig. 1. The data show that during the...
Prolonged carbohydrate alimentary challenge the animals have failed to reduce appropriately their diurnal or nocturnal intake of solid food in compensation for caloric supply provided by drinking of isotonic glucose. This is important since the average amount of calories provided by glucose drinking during the day (30 kcal) and especially night (108 kcal) was significantly greater than the amount of calories provided by the original duodenal infusion of isotonic glucose (6 kcal). As a result of the failure to compensate for this large and voluntary carbohydrate loading, considerable caloric imbalance developed during both testing periods (Fig. 1). Furthermore, glucose drinking promoted the development of significant differences in the total volume of fluid taken by animals during both the diurnal or nocturnal periods. In this regard it is important to note that when the animals were exposed diurnally or nocturnally to equiosmotic equi-volumic solution of saccharin (30 ml) failed to influence in any way subsequent intake of regular solid food. This finding is consistent with the results of drinking experiments and indicates that sweetness does not play a crucial role in the mechanism of paradoxical stimulation of food intake.

In the other experiment, prolonged infusions (30 min) of equi-osmotic equi-volumic solution of saccharin (30 ml) failed to influence in any way subsequent intake of regular solid food. This finding is consistent with the results of drinking experiments and indicates that sweetness does not play a crucial role in the mechanism of paradoxical stimulation of food intake.

Finally, the duodenal administration of the effective dose of Atromid S (100 mg/kg), which suppresses lipogenesis but by itself has no effect on normal food intake, prevented the development of paradoxical overeating by larger duodenal loads of isotonic glucose (30 ml) infused 2 hr later.

**DISCUSSION**

The results of drinking experiments clearly indicate that caloric compensation for a large voluntary carbohydrate loading by means of a reduction of food intake was not achieved during prolonged periods when the animals were exposed to isotonic glucose. Thus in comparison with the original duodenal experiment [2] the period of caloric imbalance was extended for the duration of the entire diurnal (6 hr) or nocturnal (18 hr) test periods. The fact that the intake of solid regular food in glucose exposed groups was practically the same despite the combined anorexigenic effect of marked carbohydrate loading and volume expansion indicates the potency of this phenomenon. It means that regulatory feeding mechanisms were only minimally operative (nocturnal exposure), or in fact paradoxically reversed as in the case of diurnal exposure (or following duodenal infusions). This suggests that the glucose-induced paradoxical feeding phenomenon may be of greater importance for the overall maintenance of energy balance than was originally assumed on the basis of results of duodenal infusions. This is further supported by the fact that repeated exposures actually became less effective in promoting the compensatory reduction of food intake and therefore progressively deteriorated the overall caloric imbalance induced by glucose drinking. In the case of diurnal tests, the repeated exposures actually failed completely to suppress and in fact slightly but consistently stimulated food intake. Although the mechanism of this paradoxical phenomenon is little understood, the metabolic experiments indicate that it is associated with and dependent for its expression on the excessive and prolonged insulin release. Importantly, this endocrine change is also a triggering and promoting mechanism of nocturnal overeating associated with the insulin-dependent lipogenesis. In view of clinical reports on the exaggerated insulin response to larger or prolonged alimentary glucose loads [1,4] it is most likely that the causal association of hyperinsulinemia, elevation of food intake and lipogenesis would naturally become more established after prolonged or repeated exposures to glucose solutions. This may be the case of present drinking experiments especially in the end of each exposure period (from third to fifth day).
Although the exact mechanism of paradoxical overeating remains unknown it is possible that the re-routing of the excess metabolic substrate via the insulin-dependent lipogenic routes might promote the development of a relative cellular glucoprivation as a continuous stimulus for feeding. Blockade of this preferential disposal route by inhibition of lipogenesis might considerably alter the flow of energy substrates to the cells and thus interfere with the development of paradoxical feeding response to larger glucose loads. This possibility is indicated by present results of pretreatment with Atromid S which directly support the concept on the causal role of insulin-dependent lipogenesis in the mediation of this anti-regulatory feeding phenomenon.

REFERENCES