Food Intake of Rats Given Hypertonic Solutions by Gavage and Water Intravenously[1] (34412)

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Hypertonic solutions given by gavage have been used to investigate osmotic effects on control of food intake in rats [Smith *et al.* (8); Smith (7)]. The solutes used include glucose, nonmetabolizable sugars and electrolytes. Because the depression of food intake induced by these solutions was proportional to the tonicity, the colligative properties of the solutes were considered to be the cause of this depression [Schwartzbaum and Ward (6)]. Jacobs (4) questioned this interpretation on the ground that glucose-induced depression of food intake is not accompanied by an increase of water intake. His suggestion implies that drinking is a quantitative measure of osmotic stress. However, the mechanisms of arousal of "thirst" sensation are still not well understood, although it is clear that identical osmotic pressure changes induced by different substances do not provide comparable thirst stimuli [Gilman, (3)]. Thus drinking cannot be considered the *sine qua non* for osmotic stress, and the hypothesis that glucose-induced suppression of food intake may be related to factors other than osmotic stress required further experiments. In the present study we utilized iv infusion of water concurrent with feeding in rats, to minimize the presumed osmotic stress incidental to ig glucose loading.

Method. Subjects and preparations. Seven male Charles-River rats of the Sprague-Dawley strain, 5 months old, weighing 500–545 g were used. They were individually housed in wire mesh cages with funnels for urine collection in an air-conditioned room. Powdered Purina chow and tap water were made available *ad libitum* except during the test when water was withheld.

In unpublished experiments, we found that rats of this strain consume about 40% of their daily food intake during the period between 4:00 p.m. and midnight, and during this period have a mean food intake[4] of 12.4 $\pm$ 0.3 g ($N = 85$). We decided therefore, to use the food intake during this time interval for study of the presumedly osmotic effects.

Intragastric (ig) and intrajugular (iv) catheters were implanted in each rat, the ig catheter as described by Epstein and Teitelbaum (2), the intrajugular cannulation according to Corbit (1), except that a piece of siliconized stainless steel tubing 0.5 cm in length was fitted to the intravascular end of the silastic tubing to prevent tissue reactions around the tip. The outside ends of both ig and iv catheters were threaded underneath the skin and brought out from a short incision on the scalp. Each of these ends was fitted with a piece of L-shaped metal tubing and both were anchored to the skull with dental cement fixed to 2 screws inserted into the calvarium. The openings were capped with pieces of polyethylene tubing and flame-sealed. By 7–14 days after this surgery the rats were eating normal amounts of food.

Procedure. Solutions for gavage (*i.e.*, gastric loading) were approximately equiosmotic with either 45% glucose or 8.1% NaCl (w/v). The load was 10 ml, about 2% of the body weight, given in 2 min. For iv infusion,

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[4] Mean $\pm$ standard error of mean.

TABLE I. Food Intake during 8-hr Test Following Stomach Loading with or without Intravenous Water Infusion.[a]

Rat no.	Food intake (g)					
	No solution by gavage		45% glucose, 10 ml ig		8.1% NaCl, 10 ml ig	
	No water iv	Water iv	No water iv	Water iv	No water iv	Water iv
A1	7.5	11.0	5.0	5.5	5.0	10.5
A2	8.0	11.0	5.0	3.0	3.5	5.0
A3	8.0	8.5	6.0	5.0	3.0	7.0
A4	6.0	10.0	6.0	6.0	3.0	8.5
A5	5.5	8.5	4.0	6.0	6.0	9.0
A6	6.0	9.0	5.0	5.0	4.0	7.0
A7	7.0	9.0	6.0	3.0	2.0	5.5
Mean	6.9	9.6	5.3	4.8	3.8	7.5
Correlated t	6.23		0.80		6.83	
p	<0.005		>0.25		<0.005	

[a] Volume of water infused was 25 ml by 4 hr and 40 ml in total by 8 hr. Drinking water was withheld.

sterile, pyrogen-free, distilled water was used, with the rats in their home cages and with minimal disturbance [Yin (9)]. A rate-adjustable infusion pump (Harvard Apparatus Co., model 975) was used.

After habituation to the infusion system, each rat was tested under six conditions with the following sequence: ig glucose only; ig NaCl only, no injection ig; ig glucose with iv water; ig NaCl with iv water; and no injection ig with iv water. The interval between treatments was 10 days, presumably long enough to minimize any carry-over effect. In experiments when no iv infusion was made the rat was nevertheless connected to the infusion tubing. On days with iv water infusion, as soon as the gastric loading was completed at 4:00 p.m., the iv catheters were connected, the pump was turned on, and the water infusion was continued for 8 hr. The rate and volume of infusion were selected so as to simulate the drinking response of a rat given a gastric load of 8.1% NaCl solution equal to 2% of body weight. This amounted to 25 ml by 4 hr and 40 ml by 8 hr (unpublished data). At the end of the experiment food intake was measured to 0.5 g, and urine was saved for determination of sugar by the method of Benedict or of sodium by flame photometry depending upon the substance given by gavage.

In additional experiments, rats were intragastrically loaded with either glucose or NaCl as in the previous experiment, and then after iv infusion of 5 ml of water in 1 hr a 1 ml blood sample was taken from the intrajugular catheter for determination of serum osmolality by freezing point depression.

Results. Food intake (4:00 p.m.–12:00 midnight) as a function of different gastric loads with and without continuous iv water infusion is given in Table I for individual rats. In the 3 loading situations without iv water, both glucose and NaCl suppressed food intake with respect to no-loading controls; by a correlated t test, 2-tailed, $p < 0.01$, and $p < 0.01$, respectively. The effect of NaCl was greater than that of glucose ($p < 0.05$). During iv hydration rats with glucose or NaCl loading again ate less than during control tests ($p < 0.01$, $p < 0.05$, respectively), but the intake with glucose was lower than that with NaCl loading ($p < 0.01$).

When the data on food intake with and without iv water in these three situations are compared, it is clear that iv hydration failed to alter the depression of food intake caused by glucose loading, but at least partially prevented the usual depression of intake brought on by NaCl loading. Parenteral water also enhanced food intake in tests without ig loading.

Mean serum osmolality after iv infusion of 5 ml of distilled water was 291 $\pm$ 4.2 mOsm/kg ($N = 4$) in the case of glucose load, and 311 $\pm$ 8.2 mOsm/kg ($N = 3$) in the case of NaCl load ($p < 0.10, > 0.05$). In control experiments normal serum osmolality was 303 $\pm$ 1.1 mOsm/kg [Yin (9)]. No sugar could be detected in the urine of rats with the glucose load.

Discussion. The finding that iv hydration failed to alter food intake following intragastric loading with glucose solution indicates that the glucose-induced depression of food intake is not due to an osmotic effect. That the rats were actually hydrated by the iv water was evidenced by the finding that their serum osmolality by the end of 1-hr water infusion was lower than control values.

Yin (9), studying daily feeding behavior of rats fed *ad libitum*, observed that they showed adaptation to successive daily administration of NaCl by gavage. When glucose solution was given daily in the same fashion, this adaptation did not occur. The food intake remained depressed throughout the experiment and the degree of depression was proportional to the dosage of glucose used, regardless of the tonicity. These results are consistent with the view that depression of food intake induced by glucose load is due to properties of glucose other than colligative.

In the experiments where NaCl was given by gavage, serum osmolality at the end of the 1-hr infusion of H_2O was higher than normal. This means that NaCl was being absorbed from the gut contents at a rate in excess of the rate of water infusion. These data suggest that the water infusion partially corrected both the hyperosmolarity and the depression of food intake. A more rapid administration of water might well have led to normal osmolarity and normal food intake.

The fact that with no ig load, the rats given H_2O iv ate significantly more, recalls the suggestion of Lepkovsky *et al.* (5) that the amount of food ingested depends upon how much water can be mobilized from the tissues to maintain the constancy of water concentration in the gastrointestinal contents.

Summary. Rats were prepared with chronic ig and iv catheters and fed *ad libitum.* The effect of ig loading of hypertonic glucose or NaCl on food intake was studied with and without concomitant iv infusion of distilled water. With water infusion, the depression of food intake induced by ig glucose was not affected, while the depression induced by ig NaCl was significantly attenuated. It was concluded that the depression of food intake following ig glucose is not the result of osmotic stress.

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