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BRIEF COMMUNICATION

2-deoxy-D-Glucose Induced Feeding: Relation to Diet Palatability[1]

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KANAREK, R. B. AND J. MAYER. *2-deoxy-D-glucose induced feeding: relation to diet palatability.* PHARMAC. BIOCHEM. BEHAV. 8(5) 615–617, 1978. – Adult male rats fed either ground Purina Laboratory Chow or the same diet adulterated with 0.5% quinine hydrochloride were tested for feeding in response to the administration of 2-deoxy-D-glucose (2-DG). Three doses of 2-DG were used, 250, 500, and 750 mg/kg of body weight. During a six-hr test period, rats given ground Purina Laboratory Chow ate significantly more following intraperitoneal (IP) injections of 250 and 500 mg/kg of 2-DG than following IP injections of physiological saline. Food intake of animals given Purina Chow also increased after administration of 750 mg/kg of 2-DG, but intake was not significantly different from that following saline injections. In contrast to rats maintained on the unadulterated diet, rats given quinine-adulterated chow did not increase intake over saline values during the six-hr test period following administration of 250 and 500 mg/kg of 2-DG, and actually decreased intake after injection of 750 mg/kg of 2-DG. Results are discussed with respect to the role of diet palatability in determining food intake in hungry animals.

Food intake 2-deoxy-D-glucose Quinine adulteration Diet palatability Hunger

IN AN extensive series of experiments, Jacobs and Sharma [4] reported that both dogs and cats maintained on severe food-deprivation schedules were more responsive to changes in the sensory qualities of their diets than animals given ad lib access to food. Compared to freely feeding animals, food-deprived animals showed greater increases in food intake when their diets were made more palatable, and greater decreases in intake when their diets were made less palatable. These results led Jacobs and Sharma [4] to hypothesize that contrary to the common notion that gluttony characterizes the hungry animal, hunger actually may make animals more, rather than less, discriminating in their dietary habits. Several recent studies lend support to this rather counterintuitive hypothesis. For example, Nisbett *et al.* [6] found that rats which lost weight due to forced exercise, and presumably were in a state of energy deficit, ate less of a bitter quinine-adulterated diet, and showed a greater preference for high fat diets and saccharin solutions than unexercised animals. In a recent experiment, Brandes [1] found that diet palatability also influences food intake when over-eating is induced by insulin administration. Following insulin injections, rats given a standard laboratory diet increased food intake, whereas rats provided with a quinine-adulterated diet decreased intake.

To examine further the role of diet palatability in determining food intake in hungry animals, the glucose analog 2-deoxy-D-glucose (2-DG) was given to rats maintained on either a standard laboratory diet or on the same diet adulterated with quinine. Administration of 2-DG, which decreases cellular glucose utilization in brain and other tissues by competitively inhibiting the phosphohexoseisomerase step of glycolysis [2,7] rapidly stimulates food intake in a variety of species [3, 5, 8, 9, 10]. If as Jacobs and Sharma [4] suggest, hungry animals eat primarily for taste rather than for calories, animals maintained on the quinine diet should display an attenuated response to 2-DG-induced hunger.

METHOD

Animals

Thirty-three male Sprague-Dawley rats (Charles River, CD outbred) weighing 160–180 g at the beginning of the experiment, were used. Animals were housed individually in standard wire-mesh laboratory cages in an air-conditioned room maintained on a 12-12 hr light–dark cycle (lights on: 0800 hr).

Procedure

During the first two weeks of the experiment all animals

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received ad lib access to ground Purina Laboratory Chow, provided in Wahmann (Timonium, MD) LC-306-B food cups, and water. Food and water intakes, and body weights were measured daily. The animals then were divided into two groups, matched on the basis of both food intake and body weight. Sixteen animals (Control Group) were maintained on the ground Purina diet, while 17 animals (Quinine Group) were given the ground Purina diet adulterated with 0.5% quinine hydrochloride. Daily measurements of body weights, food intakes, and water intakes were continued.

When the food intakes of animals in the Quinine Group had stabilized, testing for 2-DG induced feeding was initiated. On test days, food intakes were measured to 0.1 g each hour for a six-hr period beginning at 1030 hr. To accustom animals to the testing procedures, food intakes were measured hourly for six hr for three days with no drug injections given. On subsequent days, animals received intraperitoneal injections of either 2-DG or physiological saline. 2-deoxy-D-glucose (Sigma, St. Louis, MO) was kept frozen, and the required amount mixed with distilled water to provide a 10% solution immediately preceding its use. Three doses of 2-DG were used, 250, 500 and 750 mg/kg of body weight. All animals received the 500 mg/kg dose of 2-DG. Ten quinine and ten control animals received second injections of 750 mg/kg of 2-DG, while the remaining seven quinine animals and six control animals received second injections of 250 mg/kg of 2-DG. Thus each animal received two doses of 2-DG. On the day preceding and day following each administration of 2-DG, animals were injected with physiological saline. At least seven days separated the two injections of 2-DG received by each animal. Food intakes following 2-DG administration were compared to intakes following saline injections by using t tests for means of correlated samples.

RESULTS

Upon introduction of the quinine-adulterated diet, all animals in the Quinine Group decreased food intake and lost weight. With continued exposure to the adulterated diet, however, quinine animals slowly increased both food intake and body weight. Within ten days of presentation of the quinine diet, food intake had stabilized with quinine animals eating 85% as much per day as control animals. By the tenth day of access to the diet, quinine animals were again displaying the slow but steady weight gain characteristic of adult male rats, however, as with food intake, body weight remained below control values. From Day 10 until the end of the experiment, the weight of animals on the quinine diet was maintained at approximately 85% that of the control animals.

Although total daily food intake was different in the Quinine and Control groups, food intake during the six-hr test periods following physiological saline injections, in general, was similar for both groups. When data were averaged across all saline injections, food intake during the six-hr test period was 3.30 g for control animals, and 3.08 g for quinine animals. Following saline injections paired with 750 mg/kg of 2-DG, food intake for control animals was significantly greater than for quinine animals ($t(18) = 2.18$, $p<0.05$), however, after saline injections paired with 500 and 250 mg/kg of 2-DG, food intake was less for controls than quinine animals. For both groups, hourly food intake was generally greatest during the first hour after saline injection.

Control animals ate significantly more during the six-hr test periods following administration of 500 mg/kg ($t(15) = 5.55$, $p<0.01$) and 250 mg/kg of 2-DG ($t(5) = 4.96$, $p<0.01$) than during the six-hr periods following the corresponding saline injections (Fig. 1 – left hand panel). Although the control animals also increased food intake after injection of 750 mg/kg of 2-DG, the difference in intake between drug and saline administration was not significant. Hourly food intakes following injection of 500 mg/kg of 2-DG were significantly greater than food intakes after saline injections during the first ($t(15) = 2.07$, $p<0.05$), second ($t(15) = 2.92$, $p<0.01$), third ($t(15) = 3.26$, $p<0.01$), and fourth hr ($t(15) = 2.92$, $p<0.01$) after injection. After injection of 250 mg/kg of 2-DG, control animals increased food intake over saline values for the first ($t(5) = 3.24$, $p<0.01$), and second hr ($t(5) = 3.18$, $p<0.01$) after injection. There were no significant differences in hourly intakes between injections of 750 mg/kg of 2-DG and saline.

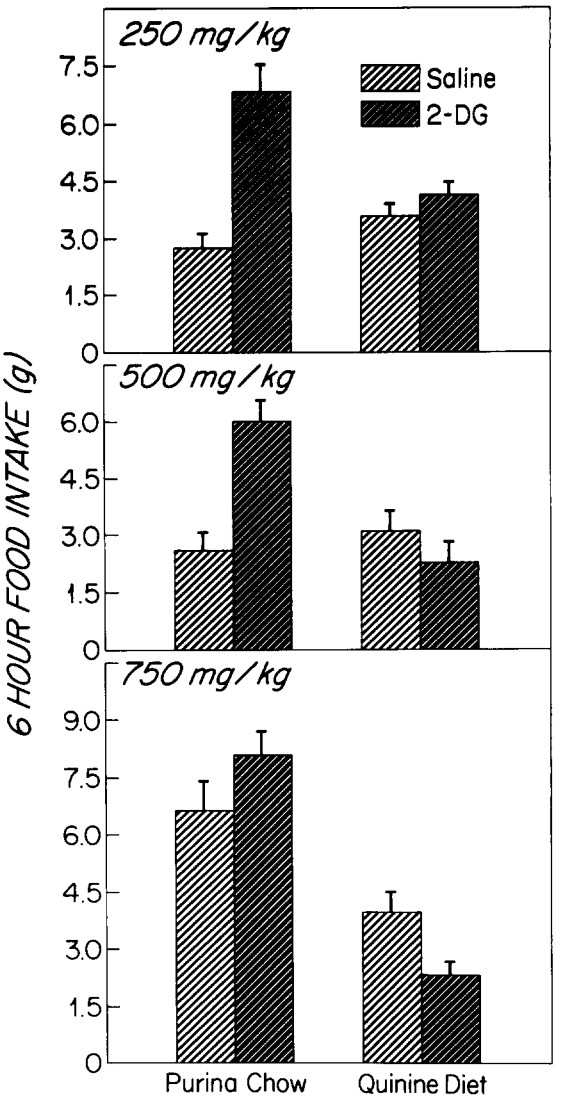

FIG. 1. Six-hour food intakes following injections of 2-DG or physiological saline of rats maintained on ground Purina Laboratory Chow or the Purina Laboratory Chow diet adulterated with 0.5% quinine hydrochloride.

In contrast to controls, animals maintained on the quinine-adulterated diet did not increase food intake when given 2-DG. After injections of 250 mg/kg and 500 mg/kg of 2-DG, total six-hr food intake for the quinine animals did not differ from intake following the corresponding saline injections, while intake after 750 mg/kg of 2-DG was actually significantly less than intake after saline injections ($t(9) = 3.98$, $p<0.01$) (Fig. 1 – right hand panel). In comparison with saline injections, hourly food intakes were significantly suppressed for the first ($t(9) = 3.01$, $p<0.01$) and second hr ($t(9) = 1.96$, $p<0.05$) after injection of 750 mg/kg of 2-DG, and for the first hr after injection of 500 mg/kg ($t(15) = 2.87$, $p<0.01$). At both doses, food intake for the fourth hr after injection was elevated above saline values ($ps<0.05$). There were no differences in food intakes between drug and saline injections for the remaining time periods.

For both control and quinine animals, food intakes during the 18-hr periods following the administration of 2-DG were similar to intakes following saline injections.

When given 750 or 500 mg/kg of 2-DG, both control and quinine animals displayed ataxia and stupor characteristic of cellular glucoprivation.

DISCUSSION

Animals maintained on a quinine-adulterated diet did not increase food intake following administration of 2-DG. This result can be contrasted with the finding of this and other studies [3, 5, 8, 9], that 2-DG reliably induced feeding in animals given standard laboratory diets. This dichotomy in response to 2-DG parallels Brandes' [1] finding that in comparison to rats given a standard diet, rats provided with a quinine-adulterated diet do not increase food intake following insulin injections. Similarly, both food-deprived animals [4], and animals forced to exercise [6] decrease food intake more than non-deprived or non-exercised animals when quinine is added to their food. Taken together with these results, the present data might be considered as support for Jacobs and Sharma's [4] hypothesis that taste is of primary importance in determining food intake in hungry animals. However, alternative explanations of the present results are also possible.

Houpt and Hance [3] found that 2-DG failed to increase feeding in food-deprived rabbits. Since in the present experiment, the Quinine Group maintained weight at approximately 85% of the Control Group's level, it could be argued that the Quinine Group responded to 2-DG like Houpt and Hance's deprived rabbits [3]. However, except during the initial dietary-induced weight loss, our animals were in positive energy balance (i.e. gaining weight) for many days, and were not subjected to episodic food deprivation prior to 2-DG injections. In addition, the six-hr baseline food intakes were equivalent in the Quinine and Control Groups, contrary to the Houpt and Hance [3] study in which food deprived animals ate considerably more than non-deprived animals under baseline conditions. Furthermore, in unpublished research from our laboratory, rats reduced in weight by a water-deprivation regime showed the typical increased feeding response to 2-DG. Therefore, the absence of a 2-DG effect in the Quinine Group probably was not due to the slightly reduced growth curve of these animals.

Another possibility is that the present results are specific to the use of quinine and not due to a more general aversive taste property of the diet. At present, we are not in a position to resolve this issue, since in unpublished research we have found the typical increased feeding response to 2-DG in rats eating an allegedly bitter sucrose octacetate-adulterated diet. Therefore, it may not be legitimate to generalize too freely concerning the effects of diet palatability on food intake in hungry animals on the basis of quinine results alone.

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