Augmented Serum Insulin Response to Glucose Infusion After the Ingestion of Konnyaku (35684)

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(Introduced by Piero P. Foà)

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It has been recognized that the plasma insulin response to orally or intestinally administered glucose is greater than that elicited by the same quantity of glucose given intravenously (1, 2), especially in gastrectomized and in mildly diabetic patients (3). The augmented release of insulin after oral glucose could be the result of the combined action of one or more hormones or of still unidentified insulin-releasing factor(s) produced by the upper gastrointestinal tract (4, 5). It is not known whether the action of these factors is associated with the process of glucose absorption or with the mechanical stimulus provided by the ingested material.

It is the purpose of this study to evaluate the effect of the mechanical stimulus to the digestive tract on insulin secretion, independently of nutrient absorption and of any concomitant elevation in the concentration of blood glucose. These experimental conditions were achieved by the ingestion of a loaf of konnyaku, made from a paste of arum root, a Japanese food which contains very few nutrients (Table I, 6).

Subjects and Methods. Sixteen healthy volunteers, 10 males and 6 females, whose ages ranged from 19 to 36 years, served as subjects. After an overnight fast, the subjects were given an intravenous infusion of glucose at the rate of 6 mg/kg/min or a 10% solution at the rate of 4.75 ml/min for 2 hr. After a 1-hr control period, the subjects received a loaf of konnyaku weighing about 250 g, cut into bite-sized pieces and consumed it within several minutes. Several days thereafter, the same procedure was repeated in three subjects in whom the parasympathetics had been blocked by 0.5 mg atropine given at the beginning of the glucose infusion and several minutes prior to the ingestion of konnyaku. In control experiments, some of the subjects were given either konnyaku alone or glucose infusion alone. Glucose was measured according to Somogyi–Nelson (7); immunoreactive insulin (IRI) with the two antibodies immunoassay of Hales and Randle (8).

Results. Figure 1 shows that during the first 30 min the mean serum glucose level increased gradually from 78.3 ± 19.1 mg/100 ml reaching a plateau of about 157 mg/100 ml in 40 min. After the ingestion of konnyaku the serum glucose concentration began to decline even though the glucose infusion was continued. On the other hand, when konnyaku was not fed, the mean serum glucose level kept increasing slightly for 90 min. The mean serum IRI concentration also increased gradually reaching a plateau about

TABLE I. Composition of Konnyaku (100 g).[a]

			Carbohydrate			Mineral			
Water	Protein	Fat	Sugar	Cellulose	Ash	Calcium	Sodium	Phosphorus	Iron
97.4	0.1	0	2.2	0.1	0.2	43	10	5	0.4

[a] Water, protein, fat, carbohydrates, and ash estimated in grams; minerals estimated in milligrams.

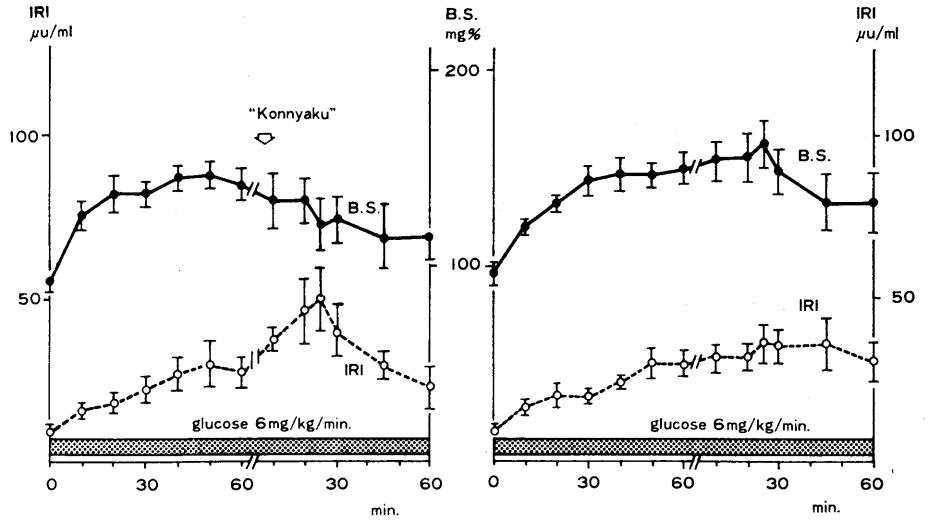

FIG. 1. Mean serum glucose and IRI responses to glucose infusion with or without ingestion of konnyaku in the same subjects.

50 min after the infusion of glucose. With feeding konnyaku there was a further rise in serum IRI levels in four of the six subjects despite the decrease in serum glucose concentration, whereas little changes in serum IRI concentration was observed in the control experiment during the corresponding period. Although the mean concentrations of serum IRI after the ingestion of konnyaku were higher than the corresponding values in the control experiment, the difference was not statistically significant.

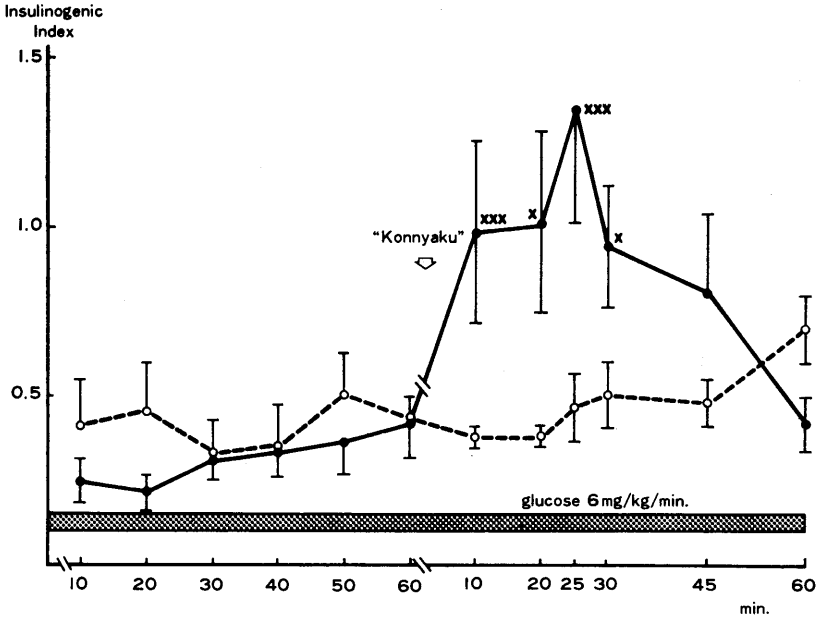

FIG. 2. Effect of konnyaku ingestion on insulinogenic index during glucose infusion. Statistical analysis based on paired comparisons. p values calculated according to the t test of Student.

x = $p<.05$;
xxx = $p<.01$.

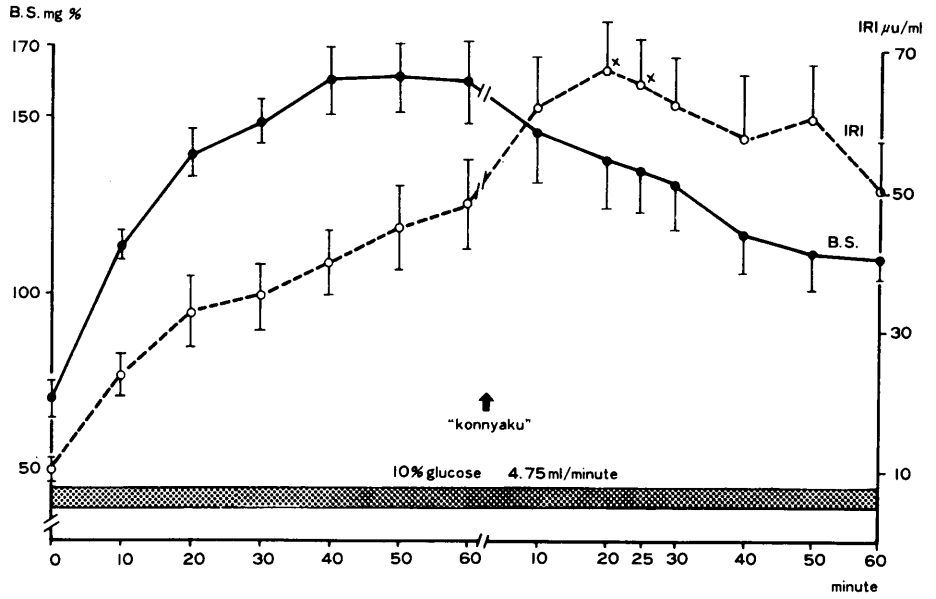

FIG. 3. Mean serum glucose and IRI responses to glucose infusion with ingestion of konnyaku. Statistical analysis based on paired comparisons. p values calculated according to the t test of Student.

x = $p<.05$ vs value before konnyaku ingestion.

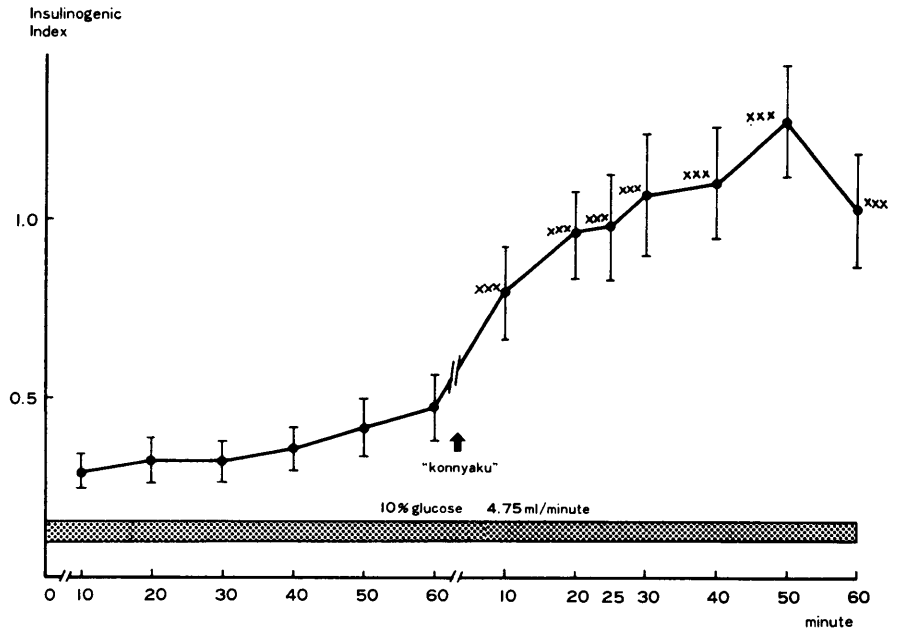

FIG. 4. Effect of konnyaku ingestion on the insulinogenic index during glucose infusion. Statistical analysis based on paired comparisons. p values were calculated according to the t test of Student.

xxx = $p<.01$ vs value before konnyaku ingestion.

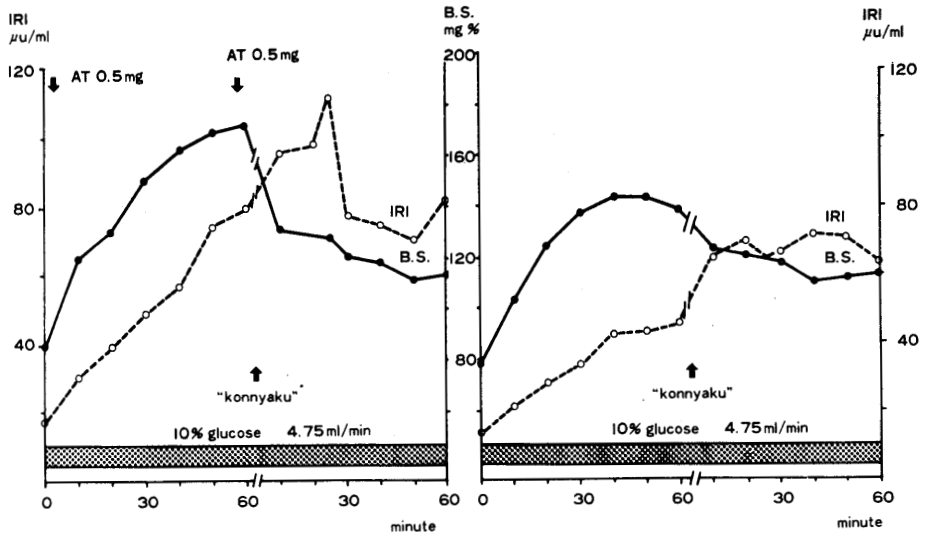

FIG. 5. Effect of atropine on the insulin response to glucose infusion augmented by the ingestion of konnyaku.

The insulinogenic index, calculated by dividing the increment in IRI concentration by the corresponding rise in glucose, increased significantly 10, 20, 25, and 30 min after konnyaku. Furthermore, after 25 and 30 min, the index was significantly higher than that observed in the control experiment at corresponding times (Fig. 2). The effect of konnyaku on serum IRI was even more pronounced in another group of 10 healthy subjects receiving glucose at the rate of approximately 475 mg/min (Fig. 3). Under these conditions, the insulinogenic index after konnyaku was significantly higher than during the control period (Fig. 4). Figure 5 demonstrates that the effect of konnyaku ingestion on serum IRI response during the glucose infusion was not abolished by parasympathet-

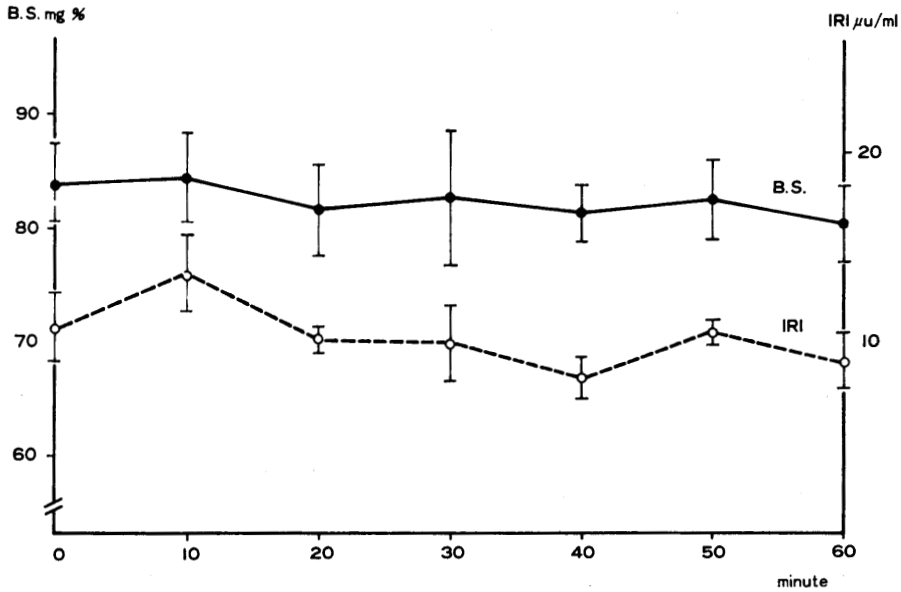

FIG. 6. Mean serum glucose and IRI responses to the ingestion of konnyaku.

ic blockade.

When konnyaku was given to seven subjects without glucose infusion, no significant changes in serum IRI and glucose concentrations were observed (Fig. 6).

Discussion. The results of this study suggest that mechanical stimuli to the digestive tract are one of the reasons why oral glucose is a more effective insulinogenic stimulus than intravenous glucose and why increasing the size of a meal, without corresponding changes in serum glucose, can increase the magnitude of the serum insulin response (9). The ingestion of konnyaku during glucose infusion caused a greater rise in serum IRI level than the glucose infusion alone even though there was a concomitant decrease in blood glucose concentration. Although these differences were not statistically significant, their combined effect resulted in a significant increase in the insulinogenic index suggesting that the mechanical effects caused by the ingestion of konnyaku augmented the sensitivity of the B cells to glucose or contributed an additional stimulation. The nature of this additional stimulation is not clear. It is unlikely that this might be the result of vagal impulses even though vagal stimulation may induce insulin secretion (10, 11), because the effect of konnyaku was not prevented by atropine. The phenomenon may be explained best by the release of one of the gastrointestinal hormones known to enhance the insulinogenic effect of glucose. Among them are secretin (12), pancreozymin, gastrin (13), and glucagon (3, 14). Although, in pharmacologic doses, these enteric hormones can stimulate the secretion of insulin from the pancreas directly, the fact that the concentration of serum insulin was not affected by the ingestion of konnyaku, unless the serum glucose level was raised, suggests that these hormones may play a permissive role by increasing the responsiveness of the B cell to glucose, thus limiting the hyperglycemic effect of a large meal.

The possible role of psychologic stimuli (15) in the physiologic release of plasma insulin cannot, of course, be excluded.

Summary. The effect of mechanical stimulation of the digestive tract was studied in 16 healthy volunteers during a continuous infusion of glucose. The ingestion of a 250-g loaf of konnyaku, a meal with insignificant nutritional value, caused an augmentation of insulin response, a decrease in blood glucose concentration and, consequently, a significant increase in the insulinogenic index. When konnyaku was given without glucose, no significant changes in serum insulin and glucose levels were observed. The augmented effect of the ingestion of konnyaku on the serum insulin response to glucose was not prevented by atropine. It is believed that humoral factors triggered by the mechanical stimulation of the digestive tract might have contributed to the observed augmentation of insulin secretion during a constant infusion of glucose.

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