

Role Played by Vagal Chemical Sensors in the Hepato-portal Region and Duodeno-intestinal Canal: An Electrophysiological Study

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Introduction

Glucose and amino acids, produced from carbohydrate and protein, suppress food intake through preabsorptive and postabsorptive mechanisms. In relation to a preabsorptive mechanism, the existence of glucoreceptors in the intestinal wall was reported by Mei (1978). For a postabsorptive mechanism, the existence of glucose sensors in the liver was first postulated by Russek (1963) on the basis of his behavioral studies. In the field of electrophysiology, Nijijima (1969, 1982) recorded electrical activity from afferent fibers from glucose sensors in the hepatic branch of the vagus nerve *in vitro* and *in vivo*. For a preabsorptive mechanism of satiation due to L-amino acids, Jeannigros (1981) identified the existence of amino acid receptors in the duodeno-intestinal canal. For a postabsorptive mechanism, the existence of amino acid sensors in the hepato-portal region was reported (Nijijima and Meguid, 1995).

This paper deals mainly with recent electrophysiological observations of glucose sensors and amino acid sensors in the hepato-portal region and duodeno-intestinal canal, and their reflex effects.

Methods

Rats were used under urethane anesthesia. Afferent signals were recorded from the nerve filament dissected from the peripheral cut end of the hepatic or celiac branch of the vagus nerve, and efferent nerve activity was recorded from the central cut end of the adrenal branch of the sympathetic nerve or pancreatic and gastric branch of the vagus nerve. Nerve activity was recorded by a pair of silver wire electrodes. A rate meter with a reset time of 5 s was used to observe the time course of nerve activity.

Glucose sensors in the hepato-portal region and duodeno-intestinal canal

Electrophysiological observation of the vagal hepatic afferents, in *in vitro* perfused guinea pig preparation indicated that firing of afferent fibers in the hepatic branch decreased following intraportal administration of glucose but not mannose or fructose (Nijijima, 1969). In an *in vivo* experiment in a rat, it was observed that an increase in the glucose content of the portal venous blood induced by the intraportal infusion (0.2 ml) of an isotonic (5%) glucose solution was accompanied by a gradual decrease in afferent discharge rate of the vagal hepatic afferents (Figure 1, top trace, right). It was further confirmed that the rates of afferent discharges were inversely related to the concentration of glucose in portal venous blood (Nijijima, 1982). This information is transmitted to the hypothalamus through the vagus nerve. It was also shown that after infusion of 15 µg of ouabain into the portal vein, an injection of glucose did not change the firing rate. This means the decrease in firing rate of hepatic afferents caused by glucose seems to be due to activation of the energy-dependent sodium pump. Suppression of the glucose-sensitive neuron in the lateral hypothalamic area (LHA) can also be explained

by this mechanism (Oomura *et al.*, 1974). Observation of the afferent activity of the celiac branch of the vagus nerve showed that an infusion of isotonic glucose (5%) solution evoked a long-lasting increase in afferent activity (Figure 1, top, left). The thinner solution did not show any clear increase.

These observations indicate that glucose sensors exist in the hepato-portal region and duodeno-intestinal canal which send afferent signals with different characteristics through the hepatic or celiac branch of the vagus nerve.

Amino acid sensors in the hepato-portal region and duodeno-intestinal canal

It has been reported that parenteral nutrition suppresses food intake in rats and this suppression is attenuated by hepatic vagotomy. For this to occur, it was hypothesized that intravenous nutrients must be sensed by hepato-portal sensors not only for glucose but also for L-amino acids that transmit signals through vagal afferent fibers to the hypothalamic food regulating areas. Our recent study (Nijijima and Meguid, 1995) shown that there are two types of amino acids with excitatory or inhibitory effects on the vagal hepatic afferents. Those are L-alanine, L-arginine, L-leucine, L-lysine, L-serine, L-tryptophan, L-valine and monosodium L-glutamate (MSG) as excitatory type. Others are L-cysteine, L-glycine, L-isoleucine, L-methionine, L-phenylalanine, L-proline and L-threonine as inhibitory type. As shown in Figure 1 (second trace), an intraportal injection of L-leucine solution (10 mM, 0.1 ml) exerts an excitatory response on the vagal hepatic afferents, and an intraduodenal infusion of a larger amount of L-leucine also evoked an excitatory response in the vagal celiac afferents. On the other hand, administrations of L-glycine solution (10 mM, 0.1 ml i.p.v. and isotonic, 3 ml i.d.) evoked inhibitory responses in the vagal hepatic afferents as well as the vagal celiac afferents (Figure 1, third trace).

All of the above-mentioned amino acids presented similar excitatory or inhibitory responses in the vagal hepatic afferents and vagal celiac afferents as well. The mechanisms for these excitatory or inhibitory responses are not clear.

Effects of amino acid deficiency on hepato-portal amino acid sensors

Effects of deficiency in amino acid were studied in L-lysine (an essential L-amino acid) deficient rat (Torii and Nijijima, 2001). To develop L-lysine deficiency, rats were offered a diet deficient in L-lysine for 7–10 days. As shown in Figure 1 (bottom, left panel), in normal rat L-lysine sensors in hepato-portal region are not responsive for L-lysine solution 0.1 mM in concentration. Then, an intraportal injection of 1 mM (0.1 ml) L-lysine solution evoked a small enhancement in vagal hepatic afferents. In L-lysine-deficient rats, an intraportal administration of L-lysine solution (0.01 mM, 0.1 ml)

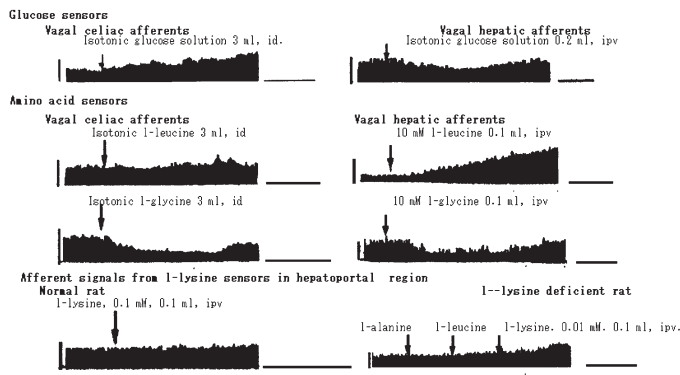


Figure 1 Different signals from glucose and amino acid sensors in the hepato-portal and duodeno-intestinal regions. Vertical bar: 100 impulses/s; horizontal bar, 30 min.

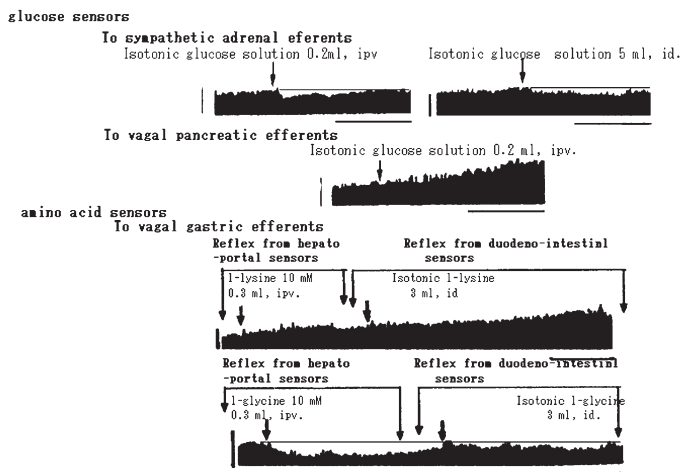


Figure 2 Reflex effects from hepato-portal and duodeno-intestinal glucose and amino acid sensors. Vertical bar: 100 impulses/s; horizontal bar, 30 min.

resulted in a clear increase in afferent activity of vagal hepatic nerve; however, injections of the same dose of L-alanine and L-leucine were without effect (Figure 1, bottom, right), suggesting that only L-lysine sensors increased their sensitivity 100-fold in L-lysine-deficient rats.

Reflex effects from hepato-portal and duodeno-intestinal glucose and amino acid sensors

Reflex effects from hepato-portal and duodeno-intestinal glucose sensors were studied. As shown in Figure 2 (top and second traces), intraportal (isotonic, 0.2 ml) and intraduodenal (isotonic solution, 5 ml) infusions of glucose solution suppressed sympathetic adrenal nerve activity and enhanced vagal pancreatic nerve activity, and hepatic vagotomy blocked these reflex responses (Nijijima, 1980). Reflex effects from hepato-portal and duodeno-intestinal L-amino acid sensors were studied on the activity of the vagal gastric efferents. The third trace in Figure 2 presents reflex effects from L-lysine sensors. An intraportal injection of L-lysine solution (10 mM, 0.1 ml) caused an increase, then following intraduodenal infusion of L-lysine solution (isotonic solution, 3 ml) also evoked long lasting enhancement in vagal gastric nerve activity. This means that stimulation of hepato-portal and duodeno-intestinal amino acid sensors with L-lysine solution evoked a reflex activation of vagal gastric nerve activity. A bottom panel of Figure 2 presents that stimulation of hepato-portal and duodeno-intestinal amino acid sensors with glycine (an inhibitory amino acid) resulted in an inhibition in nerve activity.

Conclusion

Results of experiments demonstrate the existence of glucose and amino acid sensors in the hepato-portal and duodeno-intestinal region, and their role of reflex regulation in visceral function.

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