PHYSIOLOGY

A Mechanism by Which Duodenal Contractions are Enhanced in Response to the Sympathetic Trunk Stimulation

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Stimulation of the sympathetic trunk in the thorax (5 V, 20 Hz, 1.5 msec) enhances duodenal contractions in 29% of dogs, inhibits them in 32%, and has no effect on them in 39%. The stimulatory effect is potentiated by ornid and abolished by promedol.

Key Words: *duodenum; duodenal motility; regulation*

In the middle of the 19th century Pflüger discovered that stimulation of the greater splanchnic nerve not only inhibits contractile activity of the gastrointestinal tract but also simulates it in some cases [2]. This phenomenon was observed by other investigators [10,12-14], and several hypotheses were put forward to explain its mechanism, but none of them has been generally accepted. Some researchers believe that enhanced intestinal contractions in response to the sympathetic nerve stimulation after reserpine administration result from excitation of vagal cholinergic fibers running in the mesentery [12]. Others claim that tonic contractions of the stomach arising upon stimulation of splanchnic or periarterial nerves are caused by activation of cholinergic mechanisms and α-adrenergic receptors [14]. It was suggested that enhanced gastrointestinal contractility results from the excitation of parasympathetic fibers derived from the posterior roots of the spinal cord [13]. Recently, it has been found that enhanced contractility resulting from the splanchnic nerve stimulation is abolished by atropine, but not by hexamethonium or guanethidine, and inhibition caused by the splanchnic nerve stimulation in intact animals administered a ganglioblocker is converted into stimulation [10]. From these findings it was concluded that both inhibition and stimulation result from the activation of fine afferent fibers by the axon reflex mechanism; the functional significance of these fibers is unclear [10]. We believe that increased contractile activity of the duodenum observed upon stimulation of the greater splanchnic nerve is mediated by serotoninergic nerve fibers within the sympathetic trunks [8].

The objective of this study was to examine this phenomenon in more detail in order to gain more insight into the regulation of gastrointestinal activity and into the functional organization of the autonomic nervous system.

MATERIALS AND METHODS

Acute experiments were performed on artificially ventilated mongrel dogs (body weight 7-10 kg) anesthetized with Nembutal (60 mg/kg intramuscularly). Mechanical activity of the duodenum was evaluated by recording intraduodenal pressure using a P6Ch01 polygraph equiped with an amplifier, an automatic ink recorder, and an external highly sensitive electronic sensor connected via a polyethylene tube to a

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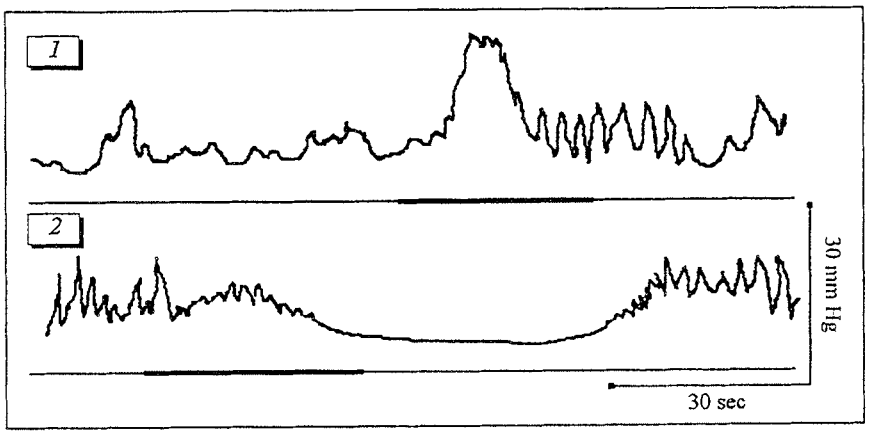

Fig. 1. Stimulatory duodenal response in one dog and inhibitory duodenal response in another dog induced by stimulation of peripheral portion of the sympathetic trunk in the thoracic cavity. *1*) enhanced duodenal contractions; 2) attenuated contractions. Two long horizontal lines are zero lines whose thick segments mark the stimulation time.

small airtight balloon (capacity 50-70 ml) filled with warm water (38°C) to two-thirds of its capacity and inserted into the duodenum. A purse-string suture was then placed around the polyethylene tube at its exit from the duodenum, and the abdominal wall was sutured or clipped. Duodenal contractions were induced by stimulation of the sympathetic trunks (ST) in the thoracic cavity in a manner not exciting parasympathetic nerve fibers of the vagal origin within sympathetic nerves in the abdominal cavity [3-6]. Electric pulses of 5, 10, and 15 V, 20 Hz, and 1.5 msec in duration (each pulse series lasting 30 sec) were applied to a peripheral portion of the ST in the area where the greater splanchnic nerve is formed by several nerve branches. The sympathetic division of the autonomic nervous system was blocked with ornid (20 mg/kg intravenously), which prevents the release of catecholamines from postganglionic nerve fibers. The HT_3 receptors of vegetative ganglia were blocked with promedol (10 mg/kg intravenously) [15].

RESULTS

Since we have hypothesized that ST contains not only inhibitory adrenergic nerve fibers but also stimulatory serotoninergic fibers of varying excitability, an attempt was made to identify the serotoninergic fibers. To this end, duodenal responses to ST stimulation with pulses of 5, 10, and 15 V (20 Hz, 1.5 msec) were applied without drugs. A total of 77 duodenal responses in 28 dogs were studied. These tests showed that ST stimulation induces inhibitory (Fig. 1, *2*) or stimulatory (Fig. 1, *1*) duodenal responses or no response at all. The number of dogs with inhibitory and stimulatory responses slightly increased with an increase in the stimulus amplitude (Fig. 2), while that with no response decreased (Table 1). After the amplitude of the stimuli had been increased from 5 to 15 V, hydrostatic pressure in the duodenal cavity rose from 9.4±1.4 mm Hg to 13.33± 1.8 mm Hg ($p<0.01$). At amplitudes of 5, 10, and 15 V, no response was observed in 39%, 21%, and 16% of the dogs, respectively. This indicates that the inhibitory and stimulatory influences in these dogs were equal, although the percentage of dogs with no response decreased considerably (from 39% to 16%) as the stimulus amplitude increased from 5 to 15 V, which was accompanied by a similar increase in the number of dogs with inhibitory and stimulatory responses. It follows that the STs have both stimulatory and inhibitory nerve fibers with a similar influence on duodenal contractility. This was surprising, since stimulatory effects are believed to be a rare event [6]. It should be stressed that a reflex-mediated enhancement of duodenal contractions by the vagus upon ST stimulation was excluded because bilateral vagotomy did not abolish the stimulatory effect. The duodenum can be stimulated by intraorgan stimulators such as cholinergic neurons which are synaptically linked to preganglionic sympathetic fibers, which was confirmed by the observation that benzohexonium (a compound blocking N-cholinergic receptors of autonomic ganglia) does not abolish stimulatory effect but even enhances it [8]. It is noteworthy that the STs in the thorax contain no sympathetic fibers of the vagus capable of enhancing duodenal contractions [8], which agrees with the findings of others [1,3]. Enhanced duodenal contractions upon ST stimulation could be attributed to the mediator peptide hormones, specifically, to substance P released from afferent fibers. However, the excitatory influence of substance P on smooth muscle is not blocked by cholinolytics [4], whereas the stimulatory effect of ST is abolished by the cholinolytic atropine [8].

Duodenal contractions enhanced immediately after the start of ST stimulation and returned to baseline level immediately after its discontinuation, which may indicate that the stimulatory effect is mediated by neural mechanisms. The afteraction time was 12±4.3 sec.

A total of 77 duodenal responses were studied in 26 dogs after injection of ornid (20 mg/kg). The ST stimulation with 5 V pulses increased duodenal contractions in 9 out of 25 dogs (36%), which was accompanied by elevation of the intraduodenal pressure from 6.8±1.0 mm Hg to 9.4±1.4 mm Hg ($p<0.01$); 16 other dogs (64%) showed no response. At a stimulus amplitude of 10 V, enhanced duodenal contractions were recorded in 16 out of 26 dogs (61.5%), weak responses were observed in 1 dog (4%), and 9 (35%) dogs did not respond to the stimulus. A similar ratio between inhibitory and stimulatory effects was observed with a stimulus amplitude of 15 V: stimulatory effect was recorded in 15 out of 26 dogs (57.7%), inhibitory effect in 2 (7.7%), and no response in 9 (34.6%).

Taken together with the published data, our results indicate that enhanced duodenal contractions in response to ST stimulation are not associated with excitation of sympathetic or parasympathetic nerve fibers. We think that the STs contain nonadrenergic and noncholinergic nerve fibers, the excitation of which stimulates peristaltics or induces it in the resting duodenum. The excitability of these fibers is higher than that of inhibitory adrenergic nerve fibers, as evidenced by the insignificant increase in the incidence of stimulatory duodenal responses (from 29% to 36%), when the amplitude of ST stimuli was increased from 5 to 15 V before ornid injection, while the occurrence of inhibitory responses increased considerably: from 32% to 48%. This implies that ST stimulation with 5-V pulses excited a vast majority of nonadrenergic and noncholinergic fibers, so that ST stimulation with pulses of higher amplitude led to excitation of predominantly inhibitory sympathetic fibers. Stimulation of the detected stimulatory nerve fibers with 10 V pulses is sufficient for the maximum effect.

The fact that ST stimulation of a given intensity failed to induce any contractile response in the duodenum before administration of ornid and stimulated duodenal contractions after the drug administration can be regarded as an additional evidence favoring the presence of stimulatory nerve fibers in the STs.

TABLE 1. Duodenal Responses in Dogs to Sympathetic Trunk Stimulation of Different Intensities

Response	Amplitude of stimulus, V		
	5 (n=28)	10 (n=24)	15 (n=25)
Enhancement	8 (28.6)	8 (33.3)	9 (35)
Inhibition	9 (32.2)	11 (45.8)	12 (48)
No change	11 (39.2)	5 (20.8)	4 (16)

Note. Percent of the total number of dogs (n) is given in parentheses.

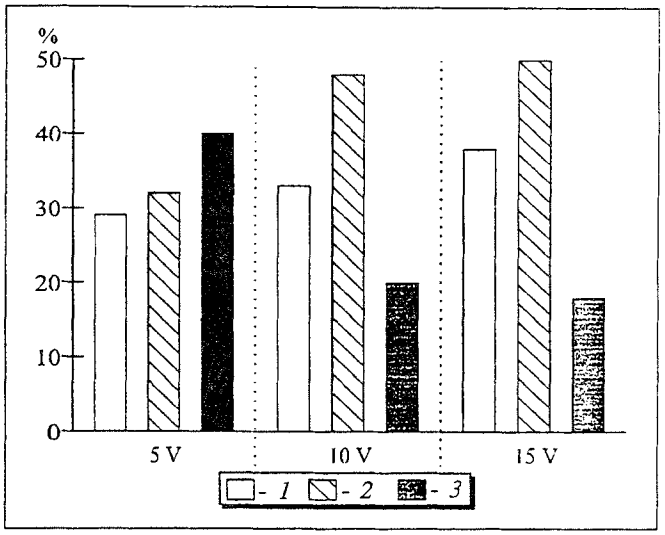

Fig. 2. Percentage of dogs with inhibitory and stimulatory duodenal responses to the sympathetic trunk stimulation with pulses of varied amplitude (5, 10, and 15 V). *1*) enhanced duodenal contractions; 2) attenuated contractions; *3*) no response because the inhibitory and excitatory influences are equal.

In fact, duodenal response was stimulated only in 8 out 24 dogs (33%) before ornid injection, while enhanced duodenal contractions were observed in 16 out of 26 dogs (62%) after the injection, since excitatory influences on the duodenum predominated.

A question arises: what is the nature of the ST nerve fibers that stimulate duodenal contractions? Based on the presence of serotoninergic neurons in the intramural neural system of the gastrointestinal tract [7,11,15] and the ability of serotonin to elicit intestinal contractions in experimental animals [9], we have hypothesized that these fibers are serotoninergic. This hypothesis was partially confirmed by our experiments in which HT_3 receptors of autonomic nerve ganglia were blocked with promedol administered against the background of ornid. These experiments were performed on 17 dogs. The peripheral segment of the right ST was stimulated with 5, 10, and 15 V pulses. Upon stimulation with 5 V pulses, attenuation of duodenal contractions was observed in 2 out of 7 dogs (28.6%), in other dogs the strength of duodenal contractions remained unchanged. Stimulation with 10 V pulses enhanced duodenal contractions only in 2 out of 11 dogs (18.2%) (*vs.* 62% before promedol injection) and attenuated them in 4 dogs (36.4%). Stimulation with 15 V pulses (n=17) did not enhance duodenal contractions in any dog and weakened them in 5 dogs (29.4%). This finding also confirms the suggestion that the excitability of sympathetic fibers is lower than that of putative serotoninergic fibers.

Thus, our results indicate that the STs contain nonadrenergic and noncholinergic nerve fibers sti-

mulating duodenal contractions, which are probably mediated by serotonin.

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