Stimulatory Effects of Centrally Injected Nitric Oxide Donors on Gastric Acid Secretion in Anesthetized Rats

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ABSTRACT—The effects of centrally injected nitric oxide (NO) donors on gastric acid secretion were investigated in continuously perfused stomach of anesthetized rats. The lateral cerebroventricular (LV) injection of NOC5 (30 – 100 μg) and NOC12 (10 – 100 μg) dose-dependently stimulated gastric acid secretion. The LV injection of NOC18 (30 μg) also stimulated gastric acid secretion. The other type of NO donor, sodium nitroprusside (3 – 30 μg, LV), also dose-dependently stimulated gastric acid secretion. The effect of NOC5 at 100 μg was blocked by carboxy-PTIO, an NO scavenger, and by cervical vagotomy. Furthermore, NOC12 (30, 100 μg) dose-dependently stimulated gastric acid secretion in pylorus-ligated conscious rats. These results suggest that centrally injected NO donors stimulate gastric acid secretion in both conscious and anesthetized rats through vagus activation.

Keywords: Nitric oxide donor, Central nervous system, Stomach, Acid secretion

Nitric oxide (NO) acts as a messenger in the central nervous system (CNS) and mediates several physiological functions (1, 2). It has been suggested that NO plays a role as a centrally acting messenger in gastrointestinal functions such as gastric motility and acid secretion (3 – 11).

As to gastric motor function, it is reported that L-arginine microinjected into the dorsal vagal complex decreases intragastric pressure in rats (3). In contrast, microinjection of L-arginine into the dorsal motor nucleus of the vagus (DMN) elicits an increase of motility in cats (4). In addition, the inhibition of NO synthase (NOS) in the brain suppresses gastric motor activity in dogs (5). In an in vitro study, treatment with NO donor and guanosine 3',5'-cyclic monophosphate of the motoneurons from the rat DMN also induces an increase in their spontaneous firing rate, which is interpreted as activation of gastric motor function through efferent cholinergic preganglionic neurons (6). Thus, centrally-acting NO modifies gastric motor functions.

As to gastric acid secretion, there are many studies on the relationship between NO and peripheral control of gastric acid secretion. It was suggested that NO shows both inhibitory (12 – 14) and stimulatory (15, 16) effects on acid secretion in peripheral nervous systems. In the CNS, it is generally accepted that endogenous NO and NO donors inhibit the gastric acid secretion stimulated by various stimulants (7 – 11). However, there are still no reports that NO in the CNS stimulates gastric acid secretion.

Depending on the concentration of NO, it is known that NO either stimulates or inhibits neurotransmitter release (17). We also showed that NO donors have a dual effect on gastric acid secretion in isolated stomach (18). The present study was undertaken to clarify whether NO in the CNS stimulates gastric acid secretion. The effects of centrally injected NO donors on gastric acid secretion were investigated in anesthetized and conscious rats.

MATERIALS AND METHODS

Animals

Male Wistar rats weighing 200 – 300 g (Takasugi Exp. Animals, Kasukabe) were housed under conditions of controlled temperature (24 ± 2°C) and a 12-h light/dark cycle (lights on at 07:00 h), for at least one week before the start of the experiment. Food and tap water were available ad libitum. Animal experiments were performed in accordance with the Guiding Principles for the Care and Use of Laboratory Animals, approved by The Japanese Pharmacological Society.

Compounds used

Sodium nitroprusside (SNP) was obtained from Wako Pure Chemical Industries (Osaka). 3-[2-Hydroxy-1-(1-
methylethyl)-2-nitrosohydrazino]-1-propanamine (NOC5), N-ethyl-2-(1-ethyl-2-hydroxy-2-nitrosohydrazino)-ethan-
amine (NOC12), 2,2'-((hydroxynitrosodihydrazino)bis-ethan-
amine (NOC18) and 2-(4-carboxyphenyl)-4,4,5,5-tetra-
methylimidazole-1-oxyl 3-oxide, sodium salt (carboxy-
PTIO) were obtained from Dojindo Laboratories (Kumamoto). These compounds were dissolved in saline. Phentol-
amine (Regitin® Inj.) was obtained from Ciba-Geigy Ltd. (Hyogo). The volume for intramuscular injection (i.m.)
was 0.5 ml/kg, and that for the lateral cerebroventricle (LV) was 5 μl/animal.

**Cannulation for LV or 4V**

Rats were anesthetized with urethane (1.35 g/kg, i.p.;
Tokyo Kasei, Tokyo) for anesthetized experiments and
with pentobarbital sodium (40 mg/kg, i.p., NEMBUTAL®;
Dainippon Pharmaceutical, Osaka) for pylorus-ligated
experiments. Animals were placed in a stereotaxic instru-
ment (SR-6; Narishige, Tokyo) in the mouth down position
(−3.3 mm). A stainless steel cannula for microinjection was
positioned unilaterally (right side) through a small hole in
the skull made by a drill. The bregma region of the parietal
skull was exposed. Stereotaxic coordinates were taken
from the atlas of Paxinos and Watson (19) and were as
follows: LV: −1.0 mm anteroposterior from the bregma,
1.3 mm lateral from the bregma and 3.8 mm dorsoventral
from horizontal skull surface. For the injection into the
4V, the implanting coordinates were as follows: −11.5 mm
anteroposterior from the bregma, 0.0 mm lateral from the
bregma and 7.5 mm dorsoventral from horizontal skull
surface. The cannula was secured by dental cement (GC
Corporation, Tokyo).

**Measurement of gastric acid secretion in anesthetized rats**

The animals were fasted for 18 h before the experiment,
but free access to water was maintained. Gastric acid
secretion was determined by the gastric perfusion method
described by Watanabe et al. (20). The esophagus was
ligated at the cervical level and a cannula was inserted
into the trachea. After laparotomy, the pylorus was ligated
and a dual cannula was inserted through a small incision
into the forestomach. The lumen was continuously perfused
with saline (adjusted to pH 5.0, 37°C) through the inlet tube
of the dual cannula at a rate of 1 ml/min. The intragastric
pressure was maintained at 5 cmH₂O. The perfusate was
continuously titrated in the reservoir with 0.02 N NaOH
to pH 5.0 using an automatic titrator (ABT-101; TOA
Electronics, Tokyo) connected to a computer system.

The animal was left for 1 h to stabilize gastric acid
secretion. After the measurement of basal acid secretion
for 30 min, the NO donor or vehicle was injected LV.
Carboxy-PTIO and NOC5 were simultaneously injected as
a mixture. Phentolamine (i.m.) was injected 30 min before
the SNP injection. In some animals, the bilateral vagus
nerves were cut at the cervical level. The amount of acid
output was expressed as ΔμEqH⁻¹/10 min of the basal
values measured 10 min prior to injection of NO donors.

**Measurement of gastric acid secretion in pylorus ligated-
rats**

At least one week after cannulation for LV, an epigastric
laparotomy was performed under light ether anesthesia.
The animals were fasted for 48 h before the experiment,
but free access to water was maintained. The pylorus was
ligated, and the abdominal incision was sutured. Then NO
donors or vehicle was injected LV as soon as possible.
Gastric juice was collected for 2 h after the pylorus-liga-
tion. The gastric juice was centrifuged at 3,000 rpm for
15 min, and the volume, pH and total acid output were
measured. After values of pH were measured, the total acid
output was determined by titrating the gastric juice with
0.02 N NaOH to pH 7.0 as described above.

**Statistics**

The values are expressed as the means ± S.E.M. The
statistical significance of differences between two groups
was assessed by Student’s t-test. Multiple comparisons
against a single control group were made by a one-way
analysis of variance followed by a Bonferroni multiple
comparisons test. Probability values at P<0.05 were con-
sidered significant.

**RESULTS**

**Effects of centrally injected NO donors on gastric acid
secretion in anesthetized rats**

Injection of NOC5 (30 – 100 μg (170.2 – 567.5 nmol)),
which was injected promptly (within 5 min) after the
dissolution, and NOC12 (10 – 100 μg (56.7 – 567.5 nmol)),
dose-dependently stimulated gastric acid secretion (Figs. 1
and 2). NOC18 (30 μg (183.8 nmol)) also stimulated
gastric acid secretion. The peak time was 50 min, 60 –
90 min and 90 – 100 min for NOC5, NOC12 and NOC18,
respectively (Fig. 3). The acid output of NOC12 had a
sustained effect for 120 min. When NOC5, NOC12 and
NOC18 of 30 μg were injected at 30 min, 120 min and 24 h
after the dissolution in saline, respectively, an increase in
gastric acid secretion was not observed (data not shown).
The stimulatory effect of NOC5 (100 μg, LV) was blocked
by carboxy-PTIO (1 mg (3.3 μmol), LV), an NO scavenger
(21) (Fig. 4). The NOC5 (100 μg, LV)-induced acid secre-
tion was abolished by cervical vagotomy (Fig. 5). The 4V
injected NOC5 (30 μg) also stimulated gastric acid secre-
tion, and the effect of 4V was similar to that of LV
(Fig. 1b).

LV injected SNP, the other type of NO donor (22), at
A dose of 3–30 µg (10.1–100.7 nmol) also evoked gastric acid secretion in a dose-dependent manner, but the action was not so potent. The total acid outputs for 90 min induced by the vehicle or SNP at 3 µg, 10 µg or 30 µg were 4.48 ± 3.24 µEq H⁺ (n = 6), 26.13 ± 11.83 µEq H⁺ (n = 4), 33.15 ± 9.76 µEq H⁺ (n = 4), 36.15 ± 6.14 µEq H⁺ (n = 4,
P < 0.05, compared with vehicle), respectively. When SNP at dose of 30 μg was injected, the respiratory insufficiency was observed in one fourth of the experimental animals. The stimulatory effect of SNP (30 μg) was significantly enhanced by phentolamine (5 mg/kg, i.m.), an α-adrenoceptor blocker (vehicle + SNP: 36.35 ± 6.14 μEq H+/90 min, n = 4; phentolamine + SNP: 103.00 ± 22.31 μEq H+/90 min, n = 4; P < 0.05, compared with SNP alone) (Fig. 6).

Effect of NOC12 on gastric acid secretion in pylorus-ligated rats

The pylorus ligation model is a simple and reliable model, which is commonly used for predicting the secretary and antisecretory activities of various agents (23–26). The present aim is to clarify whether NOC has a stimulatory effect on gastric acid secretion in conscious pylorus-ligated rats and to compare this data with results of the anesthetized rats. We decided to use the ligation time of 2 h.

As shown in Fig. 3, NOC12 showed a sustained effect in anesthetized rats. So we selected NOC12 as an NO donor in the experiment of pylorus-ligated rats. The injection of NOC12 (LV) induced increases in gastric juice volume and acid output along with a decrease in the pH (Table 1). These effects were dose-dependent.

**DISCUSSION**

**Stimulatory effects of NO donors on gastric acid secretion**

In the present study, we used NO donors such as NOCs and SNP to clarify the involvement of NO in central control
of gastric acid secretion. All NO donors used stimulated gastric acid secretion in urethane-anesthetized rats. NOC compounds are novel NO donors, and they spontaneously release NO in biological fluids without the need for a co-factor or metabolic activation (27). NOC5 and NOC12 dose-dependently stimulated gastric acid secretion (Figs. 1 and 2). NOC18 (30 μg) also stimulated gastric acid secretion. The stimulatory effects of NOC compounds were abolished when they were injected a long time after their dissolution. In addition, the effect of NOC5 was markedly inhibited by an NO scavenger, carboxy-PTIO (Fig. 4). These results suggest that NO, which is generated from NOC compounds, contributes to the secretory effects.

Next, we compared the secretory effects of three NOC compounds. The peak time of NOC compounds-induced acid secretion was observed approximately 50 min, 60–90 min and 90–100 min after the injection of NOC5, NOC12 and NOC18, respectively (Fig. 3). It is speculated that this order of acid secretion (NOC5 < NOC12 < NOC18) results from the half time of NOC compounds (NOC5: 25 min, NOC12: 100 min, NOC18: 21 h, in buffered aqueous solution at pH 7.4 and 37°C, cf., information from Dojindo Laboratories) for NO liberation in vitro.

NOC12 (30, 100 μg, LV) increased gastric juice volume and acid output along with the decrease in pH value 2 h after pylorus-ligation, showing that NOC12 also stimulated gastric acid secretion in conscious rats (Table 1). This result suggests that NO also induces the stimulatory effect on gastric acid secretion under conscious conditions.

The secretory effect of NOC5 is via activation of CNS, because cervical vagotomy blocked the NOC5-effect. This is the first report showing that centrally injected NO donors stimulate gastric acid secretion in both conscious and anesthetized rats through vagus activation. Although it has not been reported that central NO is involved in gastric acid simulation, a number of studies show the relationship between central NO and an increase of food intake. L-Arginine, which results in NO synthesis, increases food intake, while inhibitors of NOS decrease food intake and body weight in rodents (28–32). In addition, it was reported that an NOS inhibitor inhibits food intake induced by neuropeptide Y (29). Centrally injected neuropeptide Y stimulated food intake and gastric acid secretion (29, 33). Thus, central NO may be closely related to gastric acid secretion and food intake. Further studies on the physiological roles of endogenous NO in CNS are currently in progress in our laboratories.

Next, we considered the reason for the discrepancy between the present result and previous findings showing inhibition of acid secretion by NO (7–11). First, it may be due to the difference in the experimental conditions. In the present study, the NO donors were injected under the resting condition. In previous studies, they were treated under the conditions stimulated by acid secretagogues or distention. It is conceivable that NO elicits the inhibition of gastric acid secretion via the gastric sensory or sympathetic afferent nerve (34). Secondly, another possibility for the discrepancy may be due to the differences in the quantity of NO. NO dually mediates neurotransmitter release dependent on the quantity of NO, and the NO donor at some doses has a dual effect on gastric acid secretion in the isolated stomach (17, 18). Otherwise, sites of action may explain the discrepancy.

### Table 1. Effect of NOC12 on gastric acid secretion in pylorus-ligated conscious rats

| Treatment     | Dose     | No. of rats | Volume (ml) | pH       | Acid output (μEq H⁺) |
|---------------|----------|-------------|-------------|----------|---------------------|
| Vehicle (LV)  | Saline   | 7           | 1.49 ± 0.34 | 2.53 ± 0.27 | 101 ± 40            |
| NOC12 (LV)    | 30 μg/rat| 7           | 2.65 ± 0.43 | 1.96 ± 0.28 | 230 ± 76            |
| NOC12 (LV)    | 100 μg/rat| 7          | 3.14 ± 0.55*| 1.78 ± 0.21 | 278 ± 63            |

All values represent means ± S.E.M. *P<0.05, compared with vehicle.

Pathways involved in NO donors-induced gastric acid secretion

In general, sympathetic neurons do not exert a tonic inhibitory effect on gastric acid secretion, but are transiently activated by certain stimuli, leading to inhibition of gastric acid secretion (34, 35). Moreover, catecholaminergic neurons in the DMN have been reported to project selectively to the gastric corpus and may be involved in the withdrawal of cholinergic tone (36). Yokotani et al. (7) suggested that centrally injected NO donors inhibit vagally-stimulated gastric acid secretion in rats by activation of central sympathetic outflow through α-adrenoceptors. Accordingly, we added an investigation on participation of the sympathetic nerve in NO donors-induced acid secretion using phentolamine, an α-adrenoceptor blocker. As a result, the stimulatory effect of SNP (30 μg, LV) was significantly enhanced by phentolamine (Fig. 6). This result suggests that the NO donor stimulates not only the vagus nerve, but also the sympathetic nerve. The gastric acid secretion induced by SNP is thought to be obtained as the net effect.

The final integration of gastric acid secretion by central...
stimuli appears to occur in the DMN, which supplies stimulatory efferent fibers to the stomach via the vagus nerve (37, 38). We demonstrated that the DMN-vagal activation is involved in an increase of acid secretion by NO donors because the cervical vagotomy blocked the NOC5-stimulated gastric acid secretion. We injected NO donors into the LV or the 4V, and the effect of 4V injection was equipotent as that of LV injection (Fig. 1b). It is speculated that the site of action of the NO donors is in the vicinity of 4V and LV. Further studies will be required to clarify how the NO neurons in the CNS are involved in gastric acid secretion.

Conclusion
The present results showed that centrally injected NO donors stimulated gastric acid secretion via vagus activation in both conscious and anesthetized rats.

REFERENCES
1 Garthwaite J, Charles SL and Chess-Williams R: Endothelium-derived relaxing factor release on activation of NMDA receptors suggests role as intracellular messenger in the brain. Nature 336, 385 – 388 (1988)
2 Garthwaite J and Boulton CL: Nitric oxide signalling in the central nervous system. Annu Rev Physiol 57, 683 – 706 (1995)
3 Krowicki ZK, Sharkey KA, Serron SC, Nathan NA and Hornby PJ: Distribution of nitric oxide synthase in rat dorsal vagal complex and effects of microinjection of nitric oxide compounds upon gastric motor function. J Comp Neurol 377, 49 – 69 (1997)
4 Panico WH, Cavuto NJ, Kallimanis G, Nguyen C, Armstrong DM, Benjamin SB, Gillis RA and Travagli RA: Functional evidence for the presence of nitric oxide synthase in the dorsal motor nucleus of the vagus. Gastroenterology 109, 1484 – 1491 (1995)
5 Ohta D, Lee C-W, Sarna SK, Condon RE and Lang IM: Central inhibition of nitric oxide synthase modulates upper gastrointestinal motor activity. Am J Physiol 272, G417 – G424 (1997)
6 Travagli RA and Gillis RA: Nitric oxide-mediated excitatory effect on neurons of dorsal motor nucleus of vagus. Am J Physiol 266, G154 – G160 (1994)
7 Yokotani K, Murakami Y, Okuma Y and Osumi Y: Centrally applied nitric oxide donors inhibit vagally evoked rat gastric acid secretion: involvement of sympathetic outflow. Jpn J Pharmacol 74, 337 – 340 (1997)
8 Barrachina MD, Whittle BJR, Moncada S and Esplugues JV: Endotoxin inhibition of distention-stimulated gastric acid secretion in rat: mediation by NO in the central nervous system. Br J Pharmacol 114, 8 – 12 (1995)
9 Esplugues JV, Barrachina MD, Beltrán B, Calatayud S, Whittle BJR and Moncada S: Inhibition of gastric acid secretion by stress: A protective reflex mediated by cerebral nitric oxide. Proc Natl Acad Sci USA 93, 14839 – 14844 (1996)
10 Beltrán B, Barrachina MD, Méndez A, Quintero E and Esplugues JV: Synthesis of nitric oxide in the dorsal motor nucleus of the vagus mediates the inhibition of gastric acid secretion by central bombesin. Br J Pharmacol 127, 1603 – 1610 (1999)
11 Garcia-Zaragozà E, Barrachina MD, Moreno L and Esplugues JV: Role of central glutamate receptors, nitric oxide and soluble guanylyl cyclase in the inhibition by endotoxin of rat gastric acid secretion. Br J Pharmacol 130, 1283 – 1288 (2000)
12 Brown JF, Hanson PJ and Whittle BJR: The nitric oxide donor, S-nitroso-N-acetylpenicillamine, inhibits secretory activity in rat isolated parietal cells. Biochem Biophys Res Commun 195, 1354 – 1359 (1993)
13 Kim H and Kim KH: Effects of a nitric oxide donor and nitric oxide synthase inhibitors on acid secretion of isolated rabbit gastric glands. Pharmacology 53, 331 – 339 (1996)
14 Barrachina D, Calatayud S, Esplugues J, Whittle BJR, Moncada S and Esplugues JV: Nitric oxide donors preferentially inhibit neurally mediated rat gastric acid secretion. Eur J Pharmacol 262, 181 – 183 (1994)
15 Hasebe K, Horie S, Yano S and Watanabe K: Inhibitory effect of Nω-nitro-L-arginine on gastric secretion induced by secretagogues and vagal stimulation in the isolated stomach. Eur J Pharmacol 350, 229 – 236 (1998)
16 Bilski J, Konturek PC, Konturek SJ, Cieszkowski M and Czarnobilski K: Role of endogenous nitric oxide in the control of gastric acid secretion, blood flow and gastrin release in conscious dogs. Regul Pept 53, 175 – 184 (1994)
17 Prast H and Philippu A: Nitric oxide as modulator of neuronal function. Prog Neurobiol 64, 51 – 68 (2001)
18 Hasebe K, Horie S, Komasaka M, Yano S and Watanabe K: Stimulatory effects of nitric oxide donors on gastric acid secretion in isolated mouse stomach. Eur J Pharmacol 420, 159 – 164 (2001)
19 Paxinos G and Watson C: The Rat Brain in Stereotaxic Coordinates. Academic Press, Sydney (1982)
20 Watanabe K, Yano S and Minakawa Y: Morphine inhibits the gastric acid secretion stimulated by 2-deoxy-D-glucose via a central mechanism in anesthetized rats. Eur J Pharmacol 143, 293 – 298 (1987)
21 Akaike T, Yoshida M, Miyamoto Y, Sato K, Kohno M, Sasamoto K, Miyazaki K, Ueda S and Maeda H: Antagonistic action of imidazoleoxyster-N-oxides against endothelium-derived relaxing factor/-NO through a radical reaction. Biochemistry 32, 827 – 832 (1993)
22 Azula FJ, Alzola ES, Conde M, Trueba M, Macarulla JM and Marino A: Thrombin-stimulated phospholipase C activity is inhibited without visible delay by a rapid increase in the cyclic GMP levels induced by sodium nitroprusside. Mol Pharmacol 50, 367 – 379 (1996)
23 Dedieu-Chaufour C, Hertz F, Caussade F and Cloarec A: Pharmacological profile of UP 5145-52, an original antiulcer and antisecretory agent. J Pharmacol Exp Ther 259, 190 – 197 (1991)
24 Ito Y, Nakamura S, Onoda Y, Sugawara Y and Takaiti O: Effects of the new anti-ulcer drug ecabet sodium (TA-2711) on pepsin activity. I. Inactivation of enzyme protein. Jpn J Pharmacol 62, 169 – 174 (1993)
25 Kinoshita M, Saito N, Noto T and Tamaki H: Reversible inhibition of nitric oxide synthase inhibitors on acid secretion of isolated rabbit gastric glands. Br J Pharmacol 130, 1283 – 1288 (2000)
26 Wagner KA, Nandi J, King RL and Levine RA: Effects of non-steroidal antiinflammatory drugs on ulcerogenesis and gastric secretion in pylorus-ligated rat. Dig Dis Sci 40, 134 – 140 (1995)
27 Hrabie JA, Klose JR, Wink DA and Keefer LK: New nitric oxide-releasing zwitterions derived from polyamines. J Org Chem 58, 1472 – 1476 (1993)
28 Morley JE and Flood JF: Evidence that nitric oxide modulates food intake in mice. Life Sci 49, 707 – 711 (1991)
29 Morley JE and Flood JF: Competitive antagonism of nitric oxide synthetase causes weight loss in mice. Life Sci 51, 1285 – 1289 (1992)
30 Squadrito F, Calapai G, Cucinotta D, Altavilla D, Zingarelli B, Ioiculano M, Urna G, Sardella A, Campo GM and Caputi AP: Anorectic activity of $N^G$-nitro-L-arginine, an inhibitor of brain nitric oxide synthase, in obese Zucker rats. Eur J Pharmacol 230, 125 – 128 (1993)
31 Squadrito F, Calapai G, Altavilla D, Cucinotta D, Zingarelli B, Arcoraci V, Campo GM and Caputi AP: Central serotoninergic system involvement in the anorexia induced by $N^G$-nitro-L-arginine, an inhibitor of nitric oxide synthase. Eur J Pharmacol 255, 51 – 55 (1994)
32 Squadrito F, Calapai G, Altavilla D, Cucinotta D, Zingarelli B, Campo GM, Arcoraci V, Sautebin L, Mazzaglia G and Caputi AP: Food deprivation increases brain nitric oxide synthase and depresses brain serotonin levels in rats. Neuropharmacology 33, 83 – 86 (1994)
33 Geoghegan JG and Pappas TN: Central peptidergic control of gastric acid secretion. Gut 40, 164 – 166 (1997)
34 Cervero F: Sensory innervation of the viscera: peripheral basis of visceral pain. Physiol Rev 74, 95 – 138 (1994)
35 Taché Y: Central nervous system regulation of gastric acid secretion. In Physiology of the Gastrointestinal Tract, Edited by Johnson LR, Vol 2, pp 911 – 930, Raven Press, New York (1987)
36 Guo JJ, Browning KN, Rogers RC and Travagli RA: Catecholaminergic neurons in rat dorsal motor nucleus of vagus project selectively to gastric corpus. Am J Physiol 280, G361 – G367 (2001)
37 Pagani FD, Norman WP, Kasbekar DK and Gillis RA: Localization of sites within dorsal motor nucleus of vagus that affect gastric motility. Am J Physiol 249, G73 – G84 (1985)
38 Taché Y, Yang H and Yoneda M: Vagal regulation of gastric function involves thyrotropin-releasing hormone in the medullar raphe nuclei and dorsal vagal complex. Digestion 54, 65 – 72 (1993)