World Journal of Gastroenterology

Submit a Manuscript: http://www.wjgnet.com/esps/
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
DOI: 10.3748/wjg.v2.iSuppl1.20

World J Gastroenterol 1996 September 25; 2(Suppl1): 20-21
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

INVITED LECTURES

Regulation of GI motor function: Role of brain peptides

V Martinez, Y Tache

V Martinez, Y Tache, CURE: Diseases Research Center, West Los Angeles VA Medical Center. Department of Medicine and Brain Research Institute, UCLA, Los Angeles, CA 90073, United States

Author contributions: All authors contributed equally to the work.

Original title: *China National Journal of New Gastroenterology* (1995-1997) renamed *World Journal of Gastroenterology* (1998-).

Received: November 6, 1995
Revised: January 27, 1996
Accepted: July 1, 1996
Published online: September 15, 1996

Martinez V, Tache Y. Regulation of GI motor function: Role of brain peptides. *World J Gastroenterol* 1996; 2(Suppl1): 20-21 Available from: URL: http://www.wjgnet.com/1007-9327/full/v2/iSuppl1/20.htm DOI: http://dx.doi.org/10.3748/wjg.v2.iSuppl1.20

Regulation of gastrointestinal function depends largely on the integration of three systems: Central, autonomic and enteric[2,11]. A major component of the central control of gastrointestinal (GI) motor and secretory functions depends on vagal parasympathetic innervation, via modulation of circuits within the enteric nervous system, and largely through vago-vagal reflexes[2]. Retrograde and anterograde tracing techniques have established the morphological link between the GI tract and afferent and efferent vagal pathways[1]. Moreover, electrophysiological and functional approaches have shown that a number of brain peptides modulate vagal circuits at a central level, affecting GI motor functions[2].

In terms of stimulation or inhibition of GI motility or transit, only thyrotropin-releasing hormone (TRH) has been shown to act in the brain to stimulate both gastric and intestinal transit. Other brain neuropeptides have mainly an inhibitory action in gastric motility and emptying, while having varible effects on small intestine and colonic motility suggesting the involvement of multiple pathways and/or brain structures in these actions[2]. TRH nerve terminal s and fibers are located in the dorsal vagal complex and make synaptic contact with vagal preganglionic motorneurons that innervate the stomach[9]. Central TRH (after intracisternal or intracerebroventricular injection or microinjection into specific brain nuclei) stimulates gastric emptying and motility, duodenal motility and accelerates intestinal transit. The important role of the vagus as the efferent component of central TRH-induced changes in GI motor function is supported by the observations that intracisternal TRH increases efferent activity in the gastric branch of the vagus and that the motility effects of central TRH are abolished by vagotomy or atropine[14]. Microinjection techniques have determined that the dorsal motor nucleus of the vagus (DMN) is the most responsive nuclei to TRH-mediated stimulatory actions on gastric motor function[14]. TRH-containing cell bodies are localized mainly in medullary raphe nuclei (nucleus raphe magnus and obscurus) and TRH immunoreactivity in the dorsal vagal complex originates exclusively from these raphe cell bodies[5]. Functional studies also indicate that raphe nuclei play a role in the vagal dependent regulation of gastric motility through the releases of TRH and serotonin in the dorsal vagal complex[5]. The TRH stimulatory effect in the dorsal motor nucleus of the vagus is modulated by several transmitters. In particular, serotonin (5-HT), which co-exists with TRH in the same nuclei and shares a similar receptor distribution in the DMN, potentiates central TRH-induced stimulation of gastric motility[6]. Neuroanatomical and functional methods of approach have recently showed that medullary TRH plays a physiological role in the central vagal stimulation of gastric motility induced by cold exposure and 2-deoxy-D-glucose[8,16].

Another brain neuropeptide known to affect GI motor function through modulation of vagal activity is corticotropin-releasing factor (CRF). CRF plays a physiological role in integrating the central response to stress, including changes in GI motor function[12]. CRF injected into the brain ventricles or delivered into specific nuclei inhibits gastric motor activity and emptying, slows small intestine transit and stimulates colonic motility and fecal output in rats[12]. Gastric and small intestine actions depend on vagal integrity, and are abolished by vagotomy, while colonic changes seem to be mediated by modulation of sacral parasympathetic outflow[12]. Moreover, electrophysiological data show that centrally injected CRF induces a potent and long lasting decrease of single and multi-unit efferent activity of the gastric branch of the vagus, and inhibits cold exposure-induced neuronal activity in the dorsal motor nucleus of the vagus[4].

During recent years, it has been shown that the immune system plays an important role regulating GI functions through the interaction with the intrinsic and extrinsic innervation of the GI tract and through the release of CRF in the brain. Cytokines produced during immune challenges in the periphery can reach the central nervous system and those produced directly in the brain, seem to have the capacity to modulate efferent vagal activity of the GI tract. The effectiveness of centrally administered IL-1β in inhibiting vagally stimulated gastric acid secretion and lesion formation suggest that cytokines may act on the dorsal vagal complex to regulate vagal outflow to the stomach[13]. Functional data suggest that Il-1β actions are mediated through prostaglandin-and CRF-dependent mechanisms[1 0]. Moreover, microinjection into the DMN of IL-1β inhibits vagally stimulated gastric motility in anesthetized rats[7]. Similarly, tumor necrosis factor alpha (TNF-α), another cytokine, inhibits vagally stimulated gastric contractility when microinjected into the DMN[3].

These observations suggest that a number of neuropeptides (TRH, CRF) or cytokines (IL-1β, TNF-α) released at a central level

during exposure to specific environmental, metabolic or immunologic stressors have the ability to modulate vagal circuits affecting GI motor activity through direct modulation of efferent activity at a central level.

REFERENCES

1 **Berthoud HR**, Neuhuber WL. Distribution and morphology of vagal afferents supplying the digestive system. In Y. Tache, D. L. Wingated and T. F. Burks (Eds) innervation of the gut: pathophysiological implications. CRC Press, Boca Raton, 1994: 43-66

2 **Gillis RA**, Quest JA, Pagani FD, Norman WP. Control centers in the central nervous system for regulating gastrointestinal motility. In Handbood of physiology. The Gastrointestinal System, 1989: 621-683

3 **Hermann G**, Rogers RC. Tumor necrosis factor-alpha in the dorsal vagal complex suppresses gastric motility. *Neuroimmunomodulation* 1993; **2**: 74-81 [PMID: 8521142 DOI: 10.1159/000096874]

4 **Kosoyan HP**, Wei JY, Tache Y. Inhibition of gastric vagal efferent discharge by central and peripheral injection of corticotropin-releasing factor (CRF) in rats. G*astroenterology* 1994; **106**: A526

5 **Lynn RB**, Kreider MS, Miselis RR. Thyrotropin-releasing hormone-immunoreactive projections to the dorsal motor nucleus and the nucleus of the solitary tract of the rat. *J Comp Neurol* 1991; **311**: 271-288 [PMID: 1753019 DOI: 10.1002/cne.903110208]

6 **McCann MJ**, Hermann GE, Rogers RC. Dorsal medullary serotonin and gastric motility: enhancement of effects by thyrotropin-releasing hormone. *J Auton Nerv Syst* 1988; **25**: 35-40 [PMID: 3147290 DOI: 10.1016/0165-1838(88)90005-7]

7 **Morrow NS**, Quinonez G, Weiner H, Taché Y, Garrick T. Interleukin-1 beta in the dorsal vagal complex inhibits TRH analogue-induced stimulation of gastric contractility. *Am J Physiol* 1995; **269**: G196-G202 [PMID: 7653558]

8 **Okumura T**, Taylor IL, Ohning G, Taché Y, Pappas TN. Intracisternal injection of TRH antibody blocks gastric emptying stimulated by 2-deoxy-D-glucose in rats. *Brain Res* 1995; **674**: 137-141 [PMID: 7773682 DOI: 10.1016/0006-8993(95)00005-B]

9 **Rinaman L**, Miselis RR. Thyrotropin-releasing hormone-immunoreactive nerve terminals synapse on the dendrites of gastric vagal motoneurons in the rat. *J Comp Neurol* 1990; **294**: 235-251 [PMID: 2110196 DOI: 10.1002/cne.902940208]

10 **Sütö G**, Király A, Taché Y. Interleukin 1 beta inhibits gastric emptying in rats: mediation through prostaglandin and corticotropin-releasing factor. *Gastroenterology* 1994; **106**: 1568-1575 [PMID: 8194703]

11 **Taché Y**, Garrick T, Raybould H. Central nervous system action of peptides to influence gastrointestinal motor function. *Gastroenterology* 1990; **98**: 517-528 [PMID: 2104814]

12 **Taché Y**, Mönnikes H, Bonaz B, Rivier J. Role of CRF in stress-related alterations of gastric and colonic motor function. *Ann N Y Acad Sci* 1993; **697**: 233-243 [PMID: 8257013 DOI: 10.1111/j.1749-6632.1993.tb49936.x]

13 **Taché Y**, Saperas E. Potent inhibition of gastric acid secretion and ulcer formation by centrally and peripherally administered interleukin-1. *Ann N Y Acad Sci* 1992; **664**: 353-368 [PMID: 1456663 DOI: 10.1111/j.1749-6632.1992.tb39774.x]

14 **Taché Y**, Yang H. Role of medullary TRH in the vagal regulation of gastric function. In Y, Tache, D. L. Wingate and T. F. Burks (Eds). Innervation of the gut: pathophysiological implications. CRC Press, Boca Raton, 1994: 67-80

15 **Taché Y**, Yang H, Kaneko H. Caudal raphe-dorsal vagal complex peptidergic projections: role in gastric vagal control. *Peptides* 1995; **16**: 431-435 [PMID: 7544464 DOI: 10.1016/0196-9781(94)00212-O]

16 **Yang H**, Wu SV, Ishikawa T, Taché Y. Cold exposure elevates thyrotropin-releasing hormone gene expression in medullary raphe nuclei: relationship with vagally mediated gastric erosions. *Neuroscience* 1994; **61**: 655-663 [PMID: 7969936 DOI: 10.1016/0306-4522(94)90442-1]

E- Editor: Liu WX

Published by **Baishideng Publishing Group Inc**
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
http://www.wjgnet.com