

Neural Mechanism and Possible Role of Inhibition of Gastric Motility Induced by Superior Laryngeal Afferents

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Key words: electrogastrography, human, rats, relaxation, stomach, vagus, water response

Background and aims

Reduction in gastric tone can occur before food reaches the stomach. That facilitates the reservoir function of the stomach. Mechanical stimulation of the pharynx and esophagus by swallowed food itself has been assumed to induce such a gastric response. However, the relationship between the gastric reservoir function and the oropharyngeal chemoreceptor has not been clarified. The present study aimed to demonstrate that chemoreceptive afferents in the superior laryngeal nerve (SLN) facilitate the reservoir function of the stomach in rats. Furthermore, the gastric response found in rats was demonstrated to be useful to facilitate reservoir function during fluid intake in humans using an electrogastrography (EGG) method.

Gastric motor response induced by superior laryngeal afferents

All animal experiments were performed in urethane-chloralose-anaesthetized rats. Animal care was in accordance with the guidelines of the Physiological Society of Japan. Gastric motility was measured using an intragastric balloon connected to a strain-gauge pressure meter. Test solutions (0.1 ml) were administered manually toward the laryngeal surface of the epiglottis for ~10 s at room temperature through a catheter inserted into the larynx through an incision between the thyroid and circular cartilages.

Administration of water into the larynx inhibited phasic contractions of the distal stomach (Figure 1A) but 0.15 M NaCl did not

induce the inhibitory response. Bilateral sectioning of the SLN abolished the inhibitory response induced by water. Bilateral cervical vagotomies abolished the inhibitory responses, although spinal transection did not affect the inhibitory response. These inhibitory responses have been also observed in immobilized animals. The proximal stomach showed a reduction in intragastric pressure (gastric relaxation) in response to administration of water (Figure 1B). These findings suggest that water-responsive afferent neurons in the SLN suppress phasic contractions in the distal stomach and induce gastric relaxation in the proximal stomach via vagal efferent nerves (Kobashi *et al.*, 2000).

Vagal output to induce gastric motor response

The consensus of opinion is that neuroeffector transmission from the excitatory vagal pathway is cholinergic and that it is consequently blocked by atropine. Much of the tonic input to the stomach is excitatory, thus the removal of tonic inputs to the stomach causes inhibition of gastric motility. In addition, non-cholinergic and non-adrenergic (NANC) myenteric neurons, which are activated by excitation of vagal preganglionic neurons, induce the inhibition of gastric motility. To clarify the vagal output responsible for the inhibition in gastric motility induced by water fibers in the SLN, neural activities were extracellularly recorded in the dorsal motor nucleus of the vagus (DMV). The effect of peripheral muscarinic-blockade on the water-induced inhibition of gastric motility using atropine methyl nitrate, a peripherally acting muscarinic receptor antagonist, was also investigated.

Neurons in the intermediate DMV, which project to the abdominal viscera, were exclusively inhibited by water administration into the larynx or electrical stimulation of the SLN. Intravenous injection of atropine abolished the inhibition of phasic contractions in the distal stomach induced by water administration into the larynx or electrical stimulation of the SLN. Thus, inhibition of vagal preganglionic neurons evoked by laryngeal water responsive afferents likely induces inhibition of phasic contractions in the distal stomach via a cholinergic pathway (Kobashi *et al.*, 2002).

In the proximal stomach, relaxation evoked by the administration of water disappeared after intravenous injection of atropine. Relaxation evoked by electrical stimulation of the SLN was diminished in magnitude, however, still apparent after injection of atropine (Kobashi *et al.*, 2002). Thus, NANC myenteric neurons activated by excitation of vagal preganglionic neurons might be involved in the laryngeal afferent-mediated gastric relaxation. To demonstrate the NANC contribution to the relaxation of the proximal stomach, we confirmed the DMV neurons showed excitation to the electrical stimulation of the SLN by detecting *c-fos* expression after the electrical stimulation of the SLN. To identify the abdominal-projecting neurons, fluorogold was injected into the stomach wall beforehand.

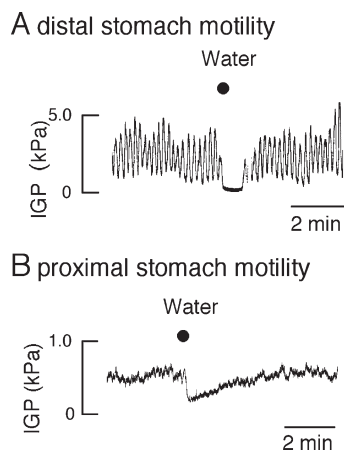


Figure 1 Gastric motor responses to the administration of water into the larynx of the rat. **(A)** Inhibition of phasic contractions of the distal stomach was observed after water-administration (filled circle). **(B)** Relaxation of the proximal stomach was observed after water-administration (filled circle). IGP: intragastric pressure.

Intermittent electrical stimulation of SLN evoked c-fos expression in fluorogold positive DMV neurons (Kobashi *et al.*, 2001). Activation of sensory fibers in the SLN might induce gastric relaxation via both cholinergic and NANC myenteric neurons.

Possible role of gastric responses in humans

To test whether the gastric response demonstrated in rats may be useful in humans, we applied an EGG method to volunteer subjects to evaluate gastric motility during fluid intake (Ashida *et al.*, 2004). EGG is both easy to use and noninvasive. Thirty-five healthy volunteers, all of whom gave informed consent, participated in this study. Experimental procedures were performed in accordance with the Ethics Committee of Kawasaki Medical School. EGGs were recorded with two cutaneous bipolar disposable Ag/AgCl electrodes. One electrode was placed midway between the umbilicus and xiphoid, and the other was placed in the midclavicular line below the left costal margin.

Before recording the human EGG, we observed rats EGG response induced by the administration of water into the larynx. A large deflection of the EGG wave was observed just after the administration of water in anesthetized rats. Therefore, we used this large deflection as an index of water response of gastric motility. A similar large deflection was observed just after voluntary drinking of water (20 ml) in the human EGG wave. Since voluntary swallowing of saliva did not change the EGG waveform, the swallowing movement itself did not affect the EGG waveform. We further observed the EGG response during reflex swallowing. The tip of a tube (OD: 5 mm) was positioned on the posterior tongue of each subject to infuse test solutions. Test solutions were delivered at a rate of 0.5 ml/s for 30 s. A few seconds after the start of infusion, the subjects reflexly swallowed. A rapid change of EGG was observed during infusion of water or citric acid (0.05 M) (Fig. 2). Infusion of 0.15 M saline did not induce any significant change. These results suggest that the change in EGG is caused by the activation of oropharyngeal chemoreceptors.

Conclusion

Chemoreceptive afferent signals in the SLN induced inhibition of gastric motility in the proximal and distal stomach of rats. These responses prevented intragastric pressures from becoming high during ingestion. The inhibitory response was mainly achieved by a reduction of tonic inputs to the stomach by inhibiting vagal preganglionic neurons, but a part of the relaxation might be mediated

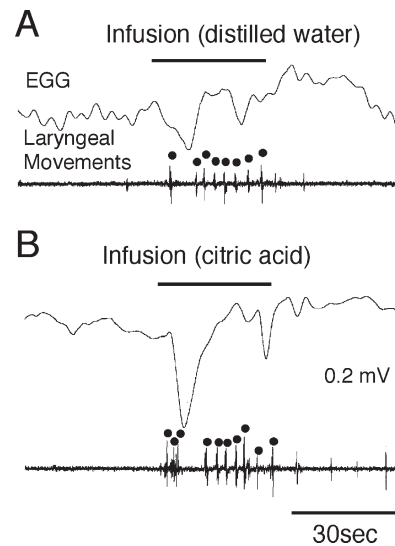


Figure 2 Change in human electrogastrography (EGG) during reflex swallowing. Infusion of water (A) or citric acid (B) induced a large change in magnitude of the EGG. Upper trace shows EGG. Lower trace shows laryngeal movements with swallowing (filled circles).

by excitation of vagal preganglionic neurons. EGG responses during reflex swallowing suggest that the gastric response found in rats may also occur in humans to facilitate reservoir function of the stomach during liquid intake.

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