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BRAIN RESEARCH

Research Report

Effects of gastric distension and infusion of umami and bitter taste stimuli on vagal afferent activity

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ABSTRACT

Until recently, sensory nerve pathways from the stomach to the brain were thought to detect distension and play little role in nutritional signaling. Newer data have challenged this view, including reports on the presence of taste receptors in the gastrointestinal lumen and the stimulation of multi-unit vagal afferent activity by glutamate infusions into the stomach. However, assessing these chemosensory effects is difficult because gastric infusions typically evoke a distension-related vagal afferent response. In the current study, we recorded gastric vagal afferent activity in the rat to investigate the possibility that umami (glutamate, 150 mM) and bitter (denatonium, 10 mM) responses could be dissociated from distension responses by adjusting the infusion rate and opening or closing the drainage port in the stomach. Slow infusions of saline (5 ml over 2 min, open port) produced no significant effects on vagal activity. Using the same infusion rate, glutamate or denatonium solutions produced little or no effects on vagal afferent activity. In an attempt to reproduce a prior report that showed distention and glutamate responses, we produced a distension response by closing the exit port. Under this condition, response to the infusion of glutamate or denatonium was similar to saline. In summary, we found little or no effect of gastric infusion of glutamate or denatonium on gastric vagal afferent activity that could be distinguished from distension responses. The current results suggest that sensitivity to umami or bitter stimuli is not a common property of gastric vagal afferent fibers.

1. Introduction

Sensory nerve pathways from the stomach to the brain are thought to be primarily sensitive to volume distension and play little role in detecting nutrients for the control of food intake (Berthoud et al., 2001; Mathis et al., 1998; Ozaki et al., 1999; Phillips and Powley, 1996; Powley and Phillips, 2004). Although evidence is sparse, reports suggest that chemical de-

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tection of ingested nutrients, especially by vagal afferent fibers, occurs further downstream in the small intestine (Jeanningros, 1982; Lal et al., 2001; Mei, 1978; Randich et al., 2000).

In recent years the view that stomach-to-brain nutritional signaling is solely volumetric has been challenged by molecular and physiological studies. Molecular work shows the presence of taste receptors in the stomach, including receptors for umami (savory taste; i.e., glutamate) and bitter stimuli (e.g., T1R3, T1R1, mGluR1, and T2Rs; Hass et al., 2010; Nakamura et al., 2010; Rozengurt, 2006). Furthermore, intragastric infusion of glutamate (150 mM) has been reported to produce activation of vagal afferent fibers in the rat within several minutes (Uneyama et al., 2006). However, this multi-unit neural response to gastric glutamate infusion occurred after an initial distension response to the volume of the infused fluid (Uneyama et al., 2006). This potential population of glutamate sensitive vagal afferents was also stimulated by intravenous infusion of serotonin (Uneyama et al., 2006).

In the current report, we investigated the separate effects of gastric distension and chemosensory stimulation on electrophysiological responses from rat gastric afferent fibers. We used two strategies to manipulate the distension responses: 1) changing the rate of infusion, and 2) closing or opening the drainage port from the stomach. We also tested the effects of denatonium, as well as glutamate, since it was reported that intragastric delivery of bitter compounds activate cFos expression in the nucleus of the solitary tract (NTS) and produce conditioned taste aversions (Glendinning et al., 2008; Hao et al., 2009).

2. Results

Fig. 1 shows the inflow and outflow ports for chemical infusion into the stomach and the location of gastric vagal afferent recordings. We recorded vagal afferent activity from two locations on the ventral trunk of the subdiaphragmatic vagus (see position 1 and 2 in Fig. 1). This was investigated because anatomical reports indicate that these separate locations have different sets of fibers, with some that travel locally between vagal branches (Prechtl and Powley, 1987, 1990). However, the only difference that we detected between these recording sites is that recording below the common hepatic branch (CHB) (position 2, Fig. 1) showed lower amplitude distension responses. The following discussion focuses on results from the recording site above the CHB (position 1, Fig. 1). See the figure caption and Section 4 for more details.

2.1. *Effects of serotonin*

In a prior study using glutamate infusion, serotonin sensitivity was a hallmark of vagal afferent recordings (Uneyama et al., 2006) and intravenous infusion of serotonin is a standard stimulus in gut vagal afferent electrophysiology experiments (e.g., Hillsley et al., 1998; Hillsley and Grundy, 1998). In

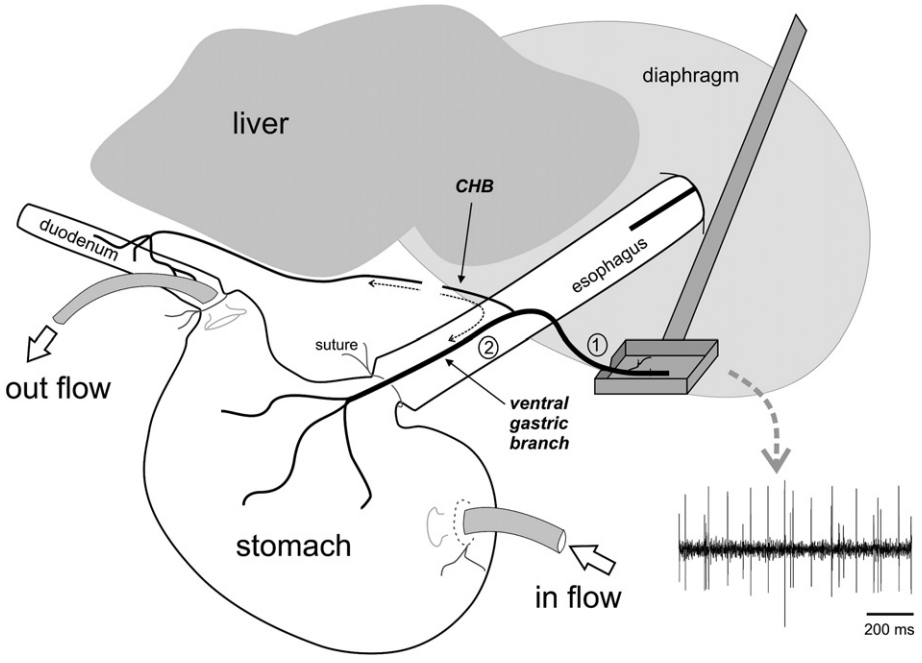

Fig. 1 – Diagram of stomach infusion and electrophysiological recording sites. Solutions were infused into stomach through a port in the fundus and drained from a port near the distal antrum. Sutures were used to secure both ports (including occlusion of pylorus) and the gastroesophageal border (placed under the nerve) to eliminate leakage from the stomach. Gastric vagal afferent responses were recorded from the cut central end of the vagus either above (position 1) or below (position 2) the common hepatic branch (CHB), which was severed (the accessory celiac branch was also ablated; not shown). The dotted line on the CHB and ventral gastric branch shows fiber tracks that travel locally (Prechtl and Powley, 1987; Prechtl and Powley, 1990). A representative electrophysiological recording is shown on the bottom right.