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T1845

Does a rectal barostat procedure induce stress in IBS patients and healthy subjects?

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The barostat can be used to study the effect of stress on pressure-volume relations and visceral perception of the rectum. However, it is not known whether the barostatprocedure (B) itself induces stress. Hence, the aim was to investigate whether a rectal B induces stress in both IBS patients and healthy subjects. Methods:Twelve IBS patients (9f, 3m, age 31-69 y) and 10 healthy females (age 18-27 y) were studied twice. The subjects underwent in random order either a 45 min B (staircase and semi-random protocol), or a rest period as a control experiment. During both B and the control experiment salivary cortisol was measured at t = -15, t = 0, t = 15, t = 30, t = 45 and t = 60 min. Changes in mood (depression, tension, vigour, hostility and tiredness) were determined simultaneously using the Profile of Mood States (POMS). Cognitive functioning (Word Learning Test, Word Recognition Test, the Verbal Fluency Test, and the Choice Reaction Task), was measured at t = 60 min in both experiments. Results: In the control group the cortisol levels showed no significant difference between the two experiments, (Wilcoxon $P > 0.169$). However, in B the patient group showed a significant increase in cortisol level ($P<0.03$) at t = 0 (immediately after insertion of the barostat probe) and t = 15 min (after the staircase protocol). During B the control group showed a significant increase in the tension subscale of the POMS t = -15 (shortly before insertion of the barostat probe) and t = 0 min ($P=0.005$ and 0.017, respectively), as well as a significant decrease in the vigour subscale at t = 45 and t = 60 min ($P=0.017$ and 0.028, respectively) compared to the control situation. In the patient group no changes in mood were observed. The cognitive tasks showed no significant differences between the two experiments in both the control and patient group. Conclusions: A rectal B induces a significant increase in salivary cortisol secretion in IBS patients but not in healthy volunteers. The POMS showed that B in healthy volunteers induces a significant increase in tension at the beginning of B, and a decrease in vigour at the end of B. The data suggest a role for the HPA-axis in the pathophysiology of IBS.

T1846

Long-Pulse and Short-Pulse Gastric Electrical Stimulation Do Not Affect Efferent Vagal Activity and Release of Regulatory Peptides in Dogs

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Background: Gastric electrical stimulation (GES) with high-frequency/ short-pulse trains (microseconds, μs) and low-frequency/ long-pulses (milliseconds, ms) can alleviate symptoms in patients with refractory gastroparesis. Both types of GES were also found to induce fundic relaxation (Xing J, et al. Gastro 2001;120:A518; Tack J, et al. Gastro 1999;116:G4733) and augment lower esophageal sphincter pressure (Xing J, et al. Gastro 2002;122:A1811). The underlying mechanisms of action remain unclear. Aim: to determine if long-pulse and short-pulse GES can modulate efferent vagal activity and release of regulatory peptides. Methods: Electrical stimulation was performed in 8 mongrel dogs by a pair of electrodes implanted in the mid body of the stomach, along the greater curvature. Three studies were performed in each animal: control (no stimulation), short pulse GES (S-GES, 14 Hz, 4mA and 330 μs with 0.1 second on and 5 seconds off) and long pulse GES (L-GES, 6cpm, 4mA and 375 ms). All studies were performed after an overnight fast, on separate days and in random order. Blood samples were collected at 15min and 0 min immediately before meal and at 15, 30 and 60 min after a standard dog food meal. GES was initiated 30min before the first blood sample and maintained throughout the study. Plasma concentrations of Pancreatic Polypeptide (PP), Gastrin, Motilin and Neurotensin (NT) were measured with Radioimmunoassay. Area under the curve (AUC) for each peptide is presented as Median with 25-75% quartiles. Statistical analysis by ANOVA, $p < 0.05$ for significance. Results: Either type of stimulus applied did not significantly affect total, fasting and postprandial AUC's of all 4 peptides. Conclusion: Gastric electrical stimulation with either long or short pulses does not significantly influence efferent vagal activity or release of regulatory peptides.

Table 1. Effect of GES on systemic peptide release, presented as total AUC (10^3)

	Baseline	S-GES	L-GES
Gastrin	6.11 [5.39-7.22]	6.73 [5.74-7.61]	6.52[5.82-6.87]
Motilin	7.89 [5.73-10.40]	6.81 [5.47-19.19]	9.27[6.98-15.17]
NT	2.27 [2.04-2.53]	2.59 [2.17-3.31]	3.00[2.820-3.41]
PP	39.47[36.44-51.78]	43.46 [35.22-48.63]	42.87[35.77-51.66]

Actual AUC: value presented 10^3; Median with 25-75% quartiles.

T1847

Alteration of Gastric Motility with Pyloric Electrical Stimulation in Dogs

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Pylorus plays an important role in the regulation of gastric emptying. The aim of this study was to investigate whether pyloric electrical stimulation (PES) had an effect on gastric emptying and gastric slow waves. Methods: The study was performed in 6 female dogs implanted with 4 pairs of electrodes on the gastric serosa, 1 pair on the pylorus and 2 pairs in the jejunum, and a duodenal fistula for the assessment of gastric emptying. The study was composed of 5 sessions (A-E) on 5 different days (A: no stimulation; B: 10cpm, 0.2ms, 5mA; C: 10cpm, 50ms, 5mA; D: 30cpm, 50ms, 5mA; E: 30cpm, 50ms, 10mA). After a 30-min recording, each dog was fed with 237ml boost and no stimulation (A) or PES (B-E) was initiated immediately after feeding and continued for 2 hrs. Gastric emptying was monitored simultaneously with gastric myoelectrical activity recording. Results: 1) Pyloric myoelectrical recording showed dual frequencies at 5.26 ± 0.08 cycles/min (cpm) and 20.13 ± 0.17cpm. The lower frequency was identical to the slow waves measured from the gastric electrodes (5.26 ± 0.09 cpm) and the higher frequency corresponded to the slow wave recorded from the jejunum (19.87 ± 0.15cpm). 2) Gastric emptying in the control session at 30-min was 56.07 ± 6.73% and was delayed with PES (method D) (22.88 ± 8.39%, $p = 0.059$ at 30-min, $p<0.05$ at 45-min and afterward) or PES (method E) (6.55 ± 1.97%, $p<0.002$ at 30-min and afterward). 3) Gastric emptying was significantly and negatively correlated with stimulation energy (r-0.673,$P<0.001$). 4) PES significantly decreased % of normal gastric slow wave 30 min after stimulation in comparison with control session (Sessions A-E: 94.0 ± 1.3%, 88.9 ± 1.9%, 87.3 ± 2.7%, 54.5 ± 13.9%, 70.1 ± 5.2, $p<0.01$, ANOVA) and energy-dependently reduced the percentage of 4-channel gastric slow wave coupling (A-E: 67.5 ± 4.5%, 64.03 ± 5.39%, 49.0 ± 10.1%, 26.8 ± 11.7%, 25.9 ± 5.3%, $p<0.005$, ANOVA); There is a significant negative correlation between slow wave coupling and stimulation energy (r-0.632,$P<0.001$) and a significant positive correlation between gastric emptying and slow wave coupling ($r=0.441$,$P<0.02$).Conclusions: PES energy-dependently delays gastric emptying which may be attributed to the impaired gastric slow wave coupling. PES may have a therapeutic potential for the treatment of obesity.

T1848

Short Pulse Gastric Electrical Stimulation Increases Vagal Activity in Rats and This Increase Is Mediated Via Vagal Afferent Pathway

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Our previous study has shown the effect of short pulse gastric electrical stimulation (GES) on vagal efferent activity. The aim of this study was to investigate whether this effect was mediated via vagal afferent pathway. Methods: Fifty male Sprague-Dawley rats were chronically implanted with 2 pairs of electrodes on gastric serosa along the greater curvature with a distance of 1.5cm between each other and the distal pair 0.5cm above the pylorus. The rats were divided into 5 groups (control group, capsaicin applied locally, perivagally and systemically, and truncal vagotomy, respectively) randomly with 10 each. Electrocardiogram and gastric slow waves were recorded for 30-min at baseline and 30-min with short pulse GES with a frequency of 20 cycles/min, amplitude of 2mA and pulse width of 300μS. These parameters were shown previously to increase vagal efferent activity in normal rats. The vagal efferent activity was assessed from the spectral analysis of the heart rate variability (HRV) signal that was derived from R-R intervals of the recorded ECG. It is known that the high-frequency component (0.8-4.0Hz in rats) in the spectrum of the HRV reflects vagal efferent activity. Spectral analysis was also performed to the recording of gastric slow waves for the derivation of the frequency and percentage of normal slow waves. Results: 1) The dominant frequency of gastric slow wave in control rats is 4.8 ± 0.4cpm, which was not different from that in vagotomized rats (4.4 ± 0.5cpm) or rats treated with capsaicin locally (4.8 ± 0.3cpm), perivagally (4.9 ± 0.2cpm) or systemically (4.7 ± 0.6cpm) ($P>0.05$, ANOVA). There was no significant difference in the percentage of regular slow wave (4-6cpm) among the 5 groups. ($P>0.05$) 2) In the control group, short pulse GES significantly increased vagal efferent activity (0.37 ± 0.08 vs. 0.31 ± 0.09 ($p<0.05$). This increase was however, not seen in any of the capsaicin treated groups or the vagatomized group. Conclusions: 1) Denervation of vagal nerve dose not disrupt the gastric slow wave, suggesting a minimal role of vagal nerves in the regulation of gastric slow waves in rats. 2) Short pulse GES increases the vagal efferent activity and this increase is mediated by vagal afferent pathway.

T1849

Phosphodiesterase Inhibitor Enhances Nerve-mediated Relaxation of the Human Stomach

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Background: Nitrergic nerves have been shown to mediate relaxation of the stomach. Recent studies suggest that one of the pathophysiology of functional dyspepsia (FD) is impaired accommodative relaxation of the proximal stomach. Enhancement of this relaxation would be a therapeutic tool for FD. Aim: The aims of this study were 1) to evaluate the role of nitrergic nerves in nerve-mediated relaxation of the human gastric tissue, and 2) to examine the effect of phosphodiesterase (PD) type 5 inhibitor, zaprinast on nerve-mediated relaxation. Methods: Human gastric tissue was obtained from the specimen of total or subtotal gastrectomy for gastric cancer. The circular and longitudinal muscle strips of the mid-gastric body were suspended in organ bath and isometric tension were measured by force transducer. Total 52 strips from 13 patients were examined. Muscle strips were pre-contracted by prostaglandine F2α (1 μM) and electrical field stimulation (EFS) was applied (2ms, 15v, 2-20Hz, 10sec train). The effects of tetrodotoxin (TTX), L-NAME, and PD inhibitor zaprinast on EFS-induced relaxation were examined. The effects of sodium nitroprusside (SNP) on resting tension, and NADPH-diaphorase activity on the human gastric tissue were also examined. Results: (1) EFS produced frequency-dependent relaxation of the human gastric circular as well as longitudinal muscle. Maximal relaxation was observed with a frequency of 20 Hz. TTX (1 μM) abolished EFS-induced relaxation ($N=6$). (2) L-NAME (1-100 μM) inhibited EFS-induced relaxation dose-dependently. L-NAME (100 μM) reduced the relaxation to 7.0+/-6.2 % of control at 2 Hz, and to 52.2+/-17.8 % of control at 20 Hz ($N=12$-20, $p<0.01$). Addition of L-arginine (3mM) restored this inhibition. SNP (1-100nM) caused dose-dependent relaxation in the presence of TTX. NADPH-diaphorase activity was observed in myenteric neurons and neuronal fibers in both circular and longitudinal muscle. (3) Zaprinast did not change the resting tension but it enhanced EFS-induced relaxation in a dose-dependent manner (0.1-10 μM). It increased the maximal relaxation (Δ tension) and duration of relaxation. Zaprinast (10 μM) caused enhancement of maximal relaxation to 128+/-13 % of control and increased area above the curve to 172+/-24 % of control at 20 Hz ($N=12$, $p<0.01$). Conclusions: These results indicate that (1) nitrergic inhibitory neurotransmission exist in the human gastric circular and longitudinal muscle, and (2) PD inhibitor enhanced these nitrergic nerve-mediated relaxation.