● G3512

NITRIC OXIDE SUPPRESSES A CALCIUM-STIMULATED CHLORIDE CURRENT IN SMOOTH MUSCLE CELLS OF THE OPOSSUM ESOPHAGUS. Fivos Vogalis, Yong Zhang & Raj K. Goyal, Harvard Med. School & West Roxbury VA, Boston MA 02132.

Nitric oxide (NO) hyperpolarizes visceral smooth muscles. In doing so NO decreases Ca^{2+} entry through voltage-gated Ca^{2+} channels and inhibits tension development. Although NO has been shown to stimulate K^+ channel currents in smooth muscle cells, the membrane hyperpolarization evoked by stimulation of nitrergic nerves in the opossum esophagus is resistant to known blockers of several classes of voltage- and Ca^{2+}-dependent K^+ channels. This suggests that NO may hyperpolarize this muscle by inhibiting a resting conductance that admits a net inward current. In the present study we investigated using the patchclamp technique the possibility that NO-mediated hyperpolarization in the circular muscle of the opossum esophagus results from the suppression of a Ca^{2+}-stimulated Cl^- current. Smooth muscle cells were dissociated from the circular layer and were bathed in high-K^+ [Ca^{2+}]-EGTA buffered solution. Macroscopic ramp currents were recorded from cell-attached patches. Contaminating K^+-channel currents were blocked with tetrapentylammonium (TPA, 200 μM) added to all solutions. Raising bath [Ca^{2+}] above 150 nM in the presence of A23187 (10 μM) activated a leak current ($I_{L\text{-}Ca}$) with an EC_{50} of 1.2 μM at -100 mV. The reversal potential (E_{rev}) of $I_{L\text{-}Ca}$ (-8.5 mV ± 1.8 mV, n=8) was significantly different ($p<0.05$) from that of the background current (+4.2 ± 1.2 mV, n=8). Equimolar substitution of 135 mM Cl^- in the pipette solution with gluconate significantly shifted E_{rev} of $I_{L\text{-}Ca}$ to + 16.6 ± 3.4 mV (n=4) ($p<0.05$ compared with background) whereas replacement of total Na^+ with $Tris^+$ suppressed $I_{L\text{-}Ca}$ but did not affect E_{rev} (-15 ± 3 mV, n=3; $p>0.05$). $I_{L\text{-}Ca}$ was inhibited by DIDS (500 μM). Both diethylenetriamine-NO adduct (DETA-NO) (200 μM), a NO• donor, and 8-bromo cGMP (100 μM) suppressed $I_{L\text{-}Ca}$ by 65 ± 16% (n=5) and 62 ± 21% (n=4) at -100 mV, respectively. The suppression of $I_{L\text{-}Ca}$ by NO, but not that elicited by 8-bromo-cGMP, was prevented by pretreatment of cells with LY83557 (100 μM). We conclude that in opossum esophageal smooth muscle NO-mediated hyperpolarization may be produced by suppression of a Ca^{2+}-stimulated Cl^- permeable conductance via formation of cGMP.

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● G3513

***IN VIVO* MODULATION OF LEFT COLONIC MOTOR FUNCTION BY A $5HT_4$ MECHANISM IN HEALTHY HUMANS.** M.R. von der Ohe, S. Klingenburg, *H. Goebell. IV. Dept. Medicine (Gastroenterology), Faculty of Clinical Medicine at Mannheim, University of Heidelberg, *Div. Gastroenterology, University of Essen, Germany.

Background: Endogenous Serotonin (5HT) plays an important role in the regulation of human colonic motor function in health and disease states (NEJM 1993;329:1073). Its effects are mediated through specific 5HT-receptors of which the $5HT_3$ subtype is known to modulate colonic motility in vivo (Gut 1994;35:536). **Aim:** To test whether a $5HT_4$ subtype-mediated mechanism participates in the regulation of human colonic motility in vivo, the effects of a selective $5HT_4$ agonist, SDZ HTF919 (Novartis, Basle, Switzerland) on human colonic motor function were assessed. **Methods:** 24 healthy volunteers (9M, 15F; mean age 31 yr) were studied by means of a combined barostat-manometry assembly placed in the descending colon (Gut 1994; 35:536). Fasting (60min), post-drug (90min; HTF919, 12mg (n=18) or placebo (n=6) p.o.) and postprandial (150min; 1000kcal liquid meal) colonic tone and phasic motility were recorded. Tone was defined as baseline barostat volume after computer-assisted elimination of phasic volume events. Postprandial values were expressed as a fraction of fasting data. Phasic pressure activity detected by manometry was calculated as the mean of values for 3 recording sites located 2, 7 and 12cm distal to the barostat balloon and expressed as a motility index [MI=ln(Σ amplitude x no. contractions)]. Statistics was by t-test. **Results (table):** HTF919 increased fasting MI while placebo had no effect. Post-drug tone was not altered in both groups (119 ± 18 vs. 128 ± 12ml). The meal increased overall colonic tone (fraction: 0.45 ± 0.11 vs. 0.49 ± 0.05, n.s.) and MI in both groups. However, HTF919 reduced the early (0-30min) but prolonged the late (90-150min) postprandial increase in tone compared with placebo.

Group	Tone			Phasic motility (MI)		
	Fasting	Fed (fraction)		Fasting	post-drug	Fed
	(ml)	early	late			
Placebo	132 ± 12	0.44 ± 0.09	0.84 ± 0.18	11.0 ± 0.8	11.8 ± 0.8	12.6 ± 0.6*
HTF919	135 ± 13	0.65 ± 0.05†	0.70 ± 0.06†	10.9 ± 0.5	12.3 ± 0.3*	12.8 ± 0.3*

Data: mean ± SEM; * $p \le 0.05$ vs. fasting; † $p \le 0.05$ vs. placebo

Conclusion: Phasic and tonic motor components in the left colon of healthy humans are modulated in vivo by a $5HT_4$ mechanism fasting and in response to endogenous stimulation by a meal. Whether selective activation of this pathway may be a future therapeutic option in the treatment of patients with impaired colonic motor function requires further clarification.

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● G3514

THE MOTOR FUNCTIONS THE HUMAN ESOPHAGEAL BODY (EB) AND LOWER ESOPHAGEAL SPHINCTER (LES) ARE REGULATED BY CERVICAL AND THORACIC SYMPATHETIC GANGLIA (SG): FUNCTIONAL EFFECTS OF A COMPUTER TOMOGRAPHY (CT)-GUIDED SELECTIVE SG BLOCK. T. von Schrenck, U. Matsui, S. Kirchhof, C. Bobrowski, H. Beck*, A. Nierhaus*, U. Rust*, H. Ohnesorge*, V. Nicolas#, J. Schulte am Esch*, H. Greten. Dep. of Medicine, Dep. of Anesthesiology*, Dep. of Radiology#, University Hospital Eppendorf, Hamburg, Germany.

The motor function of the EB and of the LES is regulated by complex mechanisms that involve an extrinsic and intramural innervation. Anatomic studies have shown that the cervical and thoracic SG are sources of the nerve supply to the EB and also to the LES. However, there are no in vivo studies on the physiological importance of this innervation in humans. **AIM:** To examine the effect of a highly selective CT-guided block of various SG on the esophageal motility in humans under in vivo conditions. **METHODS:** 8 patients with chronic pain syndromes were studied (6 with postherpetic neuralgia, two with traumatic pain). To perform a selective SG block according to the location of the pain, a G16-catheter was placed under CT-guidance directly to the various SG (patient 1: cervical SG vertebra 6/7; patient 2: cervical SG vertebra 7/8; patients 3 and 4: thoracic SG vertebra (Th) 3/4; patients 5 and 6: SG Th 4/5; patient 7: SG Th 5/6; patient 8: SG Th 6/7). The correct position was confirmed by CT after application of contrast dye. Prior to the block via the SG catheter, the contraction amplitudes of the EB and the resting pressure of the LES were determined using a Medtronic/Synectics® manometry system (8 channels, helical positions, wet swallows with 5cc water). Subsequently, 5-10 ml 0.125 % bupivacain hydrochloride were applied via the SG catheter. 30 min after the application, the manometric studies were repeated. **RESULTS:** In all patients, normal contraction profiles of the EB were recorded prior to the application of local anaesthetics. Initially, 4 patients had pathologically low LES resting pressures (< 5 mmHg). After block via the SG catheter, a significant improvement of pain scores was observed. During the block, wet swallow contraction amplitudes of the entire EB increased in each patient independently of the location of SG block (1.8-3.4-fold increase over initial pressure amplitudes, $p<0.05$). Similarly, in each patient LES resting pressures increased significantly in comprarison to the values observed prior to the block ($p<0.05$). In three of the four patients with initially low LES resting pressures, SG block caused an increase in resting pressure to values > 10 mmHg. **CONCLUSION:** Unilateral, selective block of cervical and thoracic SG causes significant changes in the motor function of the EB and LES, most likely by reducing a physiological inhibitory effect of the sympathetic innervation. These functional studies in vivo suggest that the cervical and thoracic SG are of importance for the regulation of the motor function of the EB and of the LES.

● G3515

PROXIMAL GASTRIC MOTOR FUNCTION IN REFLUX DISEASE AND AFTER LAPAROSCOPIC FUNDOPLICATION. M.K. Vu, P.J. van der Schaar, J.W.A. Straathof, C.B.H.W. Lamers, A.A.M. Masclee. Dept. of Gastroenterology-Hepatology, Leiden University Medical Center, The Netherlands.

Antireflux surgery is effective in controlling gastro-esophageal reflux (GER). After operation new symptoms such as epigastric fullness and early satiety may develop and have been related to alterations in proximal gastric motor function. It is not known whether alterations in gastric compliance and adaptive relaxation result from the antireflux procedure (fundic wrap, denervation) or are related to GER disease. Therefore we have evaluated proximal gastric motility using an electronic barostat in 12 patients after successful laparoscopic Nissen fundoplication (5 M, 7 F; age 43 ± 3 yr) in 12 patients with GERD (endoscopic esophagitis grade I-III; 7 M, 5 F; age 41 ± 4 yr) and 12 controls (7 M, 5 F; age 36 ± 4 yr). Gastric distension was performed under fasting conditions at fixed pressure levels (in 2 mmHg increments). Thereafter fundic relaxation was measured for 90 min after ingestion of a 200 ml liquid meal (300 Kcal) at minimal distending pressure (MDP) + 2 mmHg.

Results: MDP did not significantly differ post Nissen (6 ± 1 mmHg) compared to GERD patients (6 ± 1 mmHg) and controls (6 ± 1 mmHg) Neither was gastric compliance (ml/mmHg) significantly different between post Nissen patients (25 ± 3) compared to GERD patients (33 ± 4) and controls (30 ± 3). Postprandial relaxation, however, was significantly ($p<0.01$) reduced in post Nissen patients (peak bag volume increment at 15 min: 98 ± 29 ml) compared to controls (276 ± 25 ml) and GERD patients (277 ± 37 ml). The duration of postprandial fundic relaxation was significantly shorter (30 min; $p<0.01$) in post Nissen patients compared to controls (70 min). It was significantly ($p<0.01$) prolonged (> 90 min) in GERD patients.

Conclusions: Proximal gastric compliance is not affected in GERD or post fundoplication. The reduced postprandial relaxation after Nissen fundoplication is related to the procedure and not to reflux disease per se because in the latter postprandial fundic relaxation is increased and prolonged.

● G3516

ABOLITION OF CARDIOVAGAL RESPONSE TO COLORECTAL DISTENTION FOLLOWING NEONATAL CAPSAICIN. L. Wang, Y. Chen, and G. Tougas. McMaster University, IDRP, Hamilton, Ontario, Canada.

Background: Altered sensory and autonomic function may be involved in functional bowel disorders. In rats, colorectal distention produces a reflex