● G3467

ESOPHAGEAL MOTILITY IN PATHOLOGICALLY OBESE PATIENTS: A MULTIDISCIPLINARY APPROACH. E. Surrenti, G. Ciancio, S. Carloppi, R. Caramelli*, A. Coppola§, M. Lucchese°, C. Surrenti. Department of Clinical Pathophysiology, Gastroenterology Unit, *Neurophysiopathology Unit, §Nuclear Medicine Unit, University of Florence, °Surgery Unit, Italy.

In the last fifty years the standard of living in the industrialized countries led to a remarkable increase of the incidence of obesity. It is well known in the literature that this pathologic condition is associated with alteration of gastric emptying and Autonomic Nervous System (ANS) dysfunction. **AIM:** evaluate esophageal motility and ANS function in pathologically obese patients. **METHODS:** from January to June 1997 we evaluated all the obese patients referred to our institution for baryatric surgery. Exclusion criteria were: diabetes, hypertension, cardiac arhythmia, syncope, peripheral neuropathies, current or recently therapy with steroids, beta-blockers, beta-agonists, psychotrope drugs, epilepsy and Raynaud phenomenon. We enrolled in our study 22 patients (3 M and 19 F, mean age 36, range 25-57 years, Body Mass Index 45.72 ± 7.48) and 22 age and sex matched controls. Esophageal motility was evaluated by stationary manometry, scintigraphyc transit with a Tc 99 m marked bolus. Cardiovascular tests for the evaluation of ANS were: Valsalva Ratio, Deep Breathing, Sustained Handgrip and spectral analysis of the variability of the R-R interval. **RESULTS:** Compared to controls 54.5% of patients showed a reduction of esophageal pressure values at manometry, 13.7% were borderline and 31.8% were normal. Scintigraphyc esophageal transit was pathologically slow in 63% of patients, borderline in 9% and normal in 27%. Tests for ANS were normal in all patients whereas the spectral analysis of the variability of R-R interval showed an increase of the parasympathetic component both in lying and standing position compared to controls. **CONCLUSIONS:** Our data show that in obese patients there is an alteration of esophageal motility and ANS function even if they may appear to be in contrast. In our opinion these results suggest that esophageal motility is not regulated only by dichotomic system but is the result of a more complex nervous integration.

● G3468

CONTRACTILE PROTEINS THAT DISTINGUISH PHASIC FROM TONIC SMOOTH MUSCLES. Pawel T. Szymanski[1], Thomas K. Chacko[1], Artur S. Rovner[2] & Raj K. Goyal[1]; Harvard Medical School, VAMC, West Roxbury, MA 02132, [2]Dept. Mol. Physiol. & Biophys., Univ. Vermont, College of Medicine, Burlington, VT 05405-0068.

The basis of tonic versus phasic contractile phenotypes of smooth muscles are poorly understood. We used a quantitative scanning densitometry method to measure the content and isoform composition of contractile proteins in two smooth muscle types of the opossum esophagus, namely: the lower esophageal sphincter (LES), representing tonic and the esophageal body circular body (EB), representing phasic smooth muscle. The total cellular protein contents in these two types of muscle is similar and approximate 27 mg/g frozen tissue. The relative molar ratios of actin:myosin: tropomyosin:caldesmon:calponin are 14.2:0.2:1.8:0.1:0.6 in the LES and 15.5:0.3:1.8:0.4:0.5 in EB, indicating that there is no difference in the content of actin, myosin, calponin and tropomyosin. However, there is about 3-times more caldesmon in the EB as compared to LES. The relative ratios of α-:γ-contractile isoforms of actin are 0.88 in the LES and 0.25 in EB. The ratios between acidic (LC17a) and basic (LC17b) isoforms of the essential light chain of myosin is about 4.3:5.8 in the LES, as opposed to 7.3:2.7 in EB, respectively. There is no significant difference in the ratios of smooth muscle myosin (SM1) and (SM2) isoforms in the two muscle types. The level of the myosin heavy chain isoform which contains the 7 amino acid insert in myosin head is about 3-fold higher in the EB as compared to LES. In conclusion, the phasic and tonic muscles differ in the content and isoforms of contractile proteins. The phasic muscle phenotype may be related to greater abundance of LC17a, 7 amino acid inserted myosin and caldesmon and lower abundance of α-actin then the tonic phenotype.

● G3469

INVOLVEMENT OF 5-HYDROXYTRYPTAMINE IN THE CONTROL OF INTERDIGESTIVE GASTROINTESTINAL MOTILITY IN MAN. J.Tack, B.Coulie, R.Vos, B.Fischler, J.Janssens. Center for Gastroenterological Research, K.U.Leuven, Belgium.

Recently, we demonstrated that administration of peripherally acting 5-hydroxytryptamine$_1$ (5-HT$_1$) receptor agonists induces a premature intestinal phase 3 in man (Tack, AGA 1997; Tack, Gut 1998). Unfortunately, due to the lack of suitable antagonists, it is unclear whether 5-HT is involved in the control of the MMC in the small intestine in man. Selective 5-HT reuptake inhibitors act both centrally and peripherally to enhance the availability of physiologically released 5-HT. Aim: To study the effect of citalopram, a selective 5-HT reuptake inhibitor, on interdigestive gastrointestinal motility in man. Methods: In 10 healthy subjects (8 males, ages 20-29 years), antroduodenojejunal motor activity was studied by stationary, perfused catheter manometry with 3 recording orifices in the antrum, 2 in the duodenum and 2 in the jejunum. Basal interdigestive motor activity was recorded until the passage of two activity fronts. Ten minutes after the second activity front, 20 mg of citalopram was adminstered i.v. over 20 minutes. Recording continued until the passage of two or more additional activity fronts. Results (mean ± SEM) were compared by t-test or by Wilcoxon Signed Rank test. Results: Administration of citalopram induced a premature small intestinal phase 3 after 35 ± 6.4 min. The duration (6.0 ± 0.5 vs 5.8 ± 0.6 min) and the velocity of propagation of phase 3 (5.8 ± 0.2 vs 5.3 ± 0.2 cm/min) were not affected by citalopram. Before citalopram, 8 out of 20 activity fronts (40%) had a gastric origin. After citalopram only 2 of 22 activity fronts (10%) had a gastric origin ($p<0.05$). Citalopram shortened MMC cycle length from 85.4 ± 12.5 min to 49.5 ± 3.5 min ($p<0.001$). The duration of phase 1 (13.7 ± 2.4 min vs 7.1 ± 1.6 min, $p = 0.01$) and of phase 2 (66.7 ± 14.2 min vs 37.6 ± 6.5 min, $p < 0.05$) of the MMC-cycle was significantly shortened by citalopram. Citalopram significantly increased the motility index during phase 2 in the stomach (3.64 ± 0.25 vs 4.20 ± 0.15 ml*mm Hg/min, $p = 0.05$) and in the small intestine (4.40 ± 0.12 vs 4.77 ± 0.17 ml*mm Hg/min, $p < 0.05$). Conclusions: In the interdigestive state in man, oral administration of the selective 5-HT reuptake inhibitor citalopram induces a premature phase 3 in the small intestine while gastric activity fronts are suppressed. Phase 2 motility is stimulated both in the stomach and in the small intestine after citalopram. These data suggest that release of 5-HT, probably at the level of the enteric nervous system, is involved in the control of interdigestive motility in man.

● G3470

DISTRIBUTION AND ACTIONS OF ORPHANIN IN RAT GASTROINTESTINAL TRACT. T Takahashi, D Bagnol, A Yazdani, Y Li, SJ Watson and C Owyang. Department of Internal Medicine and Mental Health Research Institute, University of Michigan, Ann Arbor, MI.

The newly discovered peptide Orphanin FQ (OFQ) is the endogenous ligand of the OFQ receptor, which shares high structural similarities with the opioid receptors. OFQ acts as a neurotransmitter in the brain by modulating nociceptive and locomotor behavior (Science, 270, 792-794, 1995). However, the physiological role of OFQ in the gastrointestinal (GI) tract remains unknown. In this study we investigated the distribution and actions of OFQ in various tissues of the rat GI tract. Immunohistochemistry demonstrated the presence of OFQ-immunopositive cells and fibers in the myenteric plexus throughout the GI tract. OFQ (10^{-9}-10^{-6}M) significantly reduced electrical field stimulation (EFS: 10 Hz, 0.5 msec)- evoked muscular contraction in a dose dependent manner in the ileum and stomach but not in the colon. ^{3}H-acetylcholine release in response to EFS was reduced to 45% and 88% of control by OFQ (3 x 10^{-7}M) in the ileum and stomach respectively, but not in the colon. In contrast, OFQ (10^{-10} - 10^{-7}M) caused dose dependent contractions both in colonic longitudinal and circular muscle strips. Intravenous administration of OFQ (3 pmol/kg-3 nmol/kg) stimulated colonic contractions in a dose dependent manner in vivo with OFQ 3nmol/kg producing a 715% increase of basal contraction. In contrast, intracerebroventricular administration of OFQ (3 pmol/kg-100 pmol/kg) failed to stimulate colonic contraction. Furthermore, extrinsic denervation had no effect on OFQ evoked colonic contraction. OFQ failed to cause any contractions in the stomach or ileum both in vivo and vitro. OFQ-induced colonic contractions were not affected by pretreatment with naloxone, atropine, guanethidine, indomethacin, L-NAME, apamin, VIP antagonist, substance P antagonist, GABA antagonist, 5HT antagonist, or CGRP antagonist both in vivo and in vitro. Tetrodotoxin and serosal application of benzalkolium chloride (which ablates the myenteric plexus) abolished OFQ-induced contraction both in vivo and in vitro, suggesting that OFQ action is mediated via the myenteric plexus. In situ hybridization showed that OFQ receptors are expressed in abundance in the myenteric plexus but not in the muscle layers. In conclusion, OFQ and OFQ receptors are expressed in the myenteric plexus throughout the GI tract, however the mechanisms of action differ depending on the region. OFQ inhibits cholinergic transmission in the stomach and ileum, whereas OFQ causes contraction in the colon, probably by inhibiting a novel inhibitory neural pathway.