MODIFICATION OF COLONIC RESPONSE TO EATING (CRE) INDUCED BY PINAVERIUM BROMIDE (PB) IN CONTROL AND IBS PATIENTS. Bouchoucha M*, Odinot J-M*, Landi B*, Dyard P** , Cugnenc P-H*, Barbier J-P*. *Département de Gastroentérologie, Hôpital Laënnec, 42, rue de Sèvres F75007 Paris.* * Laboratoires LATEMA 92 Suresnes.

Pinaverium Bromide is a calcium channel blocker used in the treatment of IBS. It was showed that PB, intravenous administrated, inhibits CRE. *AIM* : The aim of this study was to describe the modification of the CRE induced by oral PB, in term of transit, in control and IBS patients. *METHODS* . In a double-blind study (placebo *vs* PB, 100 mg/day, 3 times a day) in 73 volunteer subjects (30 healthy controls and 43 patients with IBS according the Rome criteria), an evaluation of the CRE after ingestion of a standard test meal of 1000 Kcal, was performed by study of the movement of radiopaque markers. *RESULTS* : After meal, the count of markers (M±SEM) in the different segments show that in controls, PB only increases the number of markers in the rectosigmoid area (13.9±2.3 *vs* 17.6±2.4, $p<0.03$). In IBS patients, PB decreases the number of markers in the ascending colon (20.7±2.2 *vs* 19.0˜2.2, $p<0.05$) and increases the number of markers in the rectosigmoid area (16.3±1.9 *vs* 18.7±2.1, $p<0.01$). In contrast, before eating, PB induces no significant variation. *CONCLUSION* : The clinical action of PB could result of its action on CRE.

● EFFECT OF FEDOTOZINE ON GASTRIC NOCICEPTION ASSESSED BY A REFLEXOLOGIC TECHNIQUE. D. Bouhassira, B. Coffin, R. Chollet, B. Fraitag, J. Genève, J.C. Willer, R. Jian. INSERM U290 & U161, Hôpital Saint-Louis, and Institut de Recherche Jouveinal, Paris, France.

Fedotozine, a peripheral kappa agonist, has been shown to increase discomfort threshold to gastric distension, and thus to decrease gastric nociception. The aim of this study was to assess this effect with a reflexologic technique, based on the inhibition of a spinal cutaneo-muscular flexion reflex (RIII), that allows an accurate and objective evaluation of visceral nociception (1) and does not involve suprathalamic structures and nonspecific emotional or stressful reactions.

Methods: 10 healthy subjects, included in a double blind cross over study, received fedotozine (F, 30 mg tid) and a placebo (P) in a randomized order during 1 week. Experiments were performed before (basal) and at the end (day 7) of each therapeutic sequence. RIII was continuously elicited by electrical stimulation of the sural nerve and recorded from the ipsilateral biceps femoris muscle. Isovolumic gastric distensions (1000 mL) were carried out with an electronic barostat during 3 min. Results (m ± SD) were evaluated by a 3 way analysis of variance.

Results: RIII intensity (percentages of basal values)

	Placebo sequence		Fedotozine sequence	
	Basal(BP)	Placebo(P)	Basal(BF)	Fedotozine(F)
1st min	49 ±16	51±21	46±18	72±38*
2nd min	38 ±10	51±19*	36±20	60±31**
3rd min	47 ±16	62±15*	41±15	56±31

* : p = 0.008 vs. BP, BFand P ; ** p = 0.012 vs. BP and BF.

Gastric distension inhibited the RIII reflex in all circumstances. Fedotozine significantly decreased RIII inhibition, but this effect was limited to the first minute of the distension period.

Conclusion: These results confirm that fedotozine decreases gastric nociception by acting on afferent visceral pathways. They show that, under the present experimental conditions, its effect is limited to the induction of nociception. These results illustrate the interest of the RIII technique to asses the pharmacological action of drugs on visceral sensitivity.

(1) Bouhassira et al, Gastroenterology, 1994, 107, 985-992.

● **USE OF ECHO PLANAR IMAGING (EPI) TO ASSESS THE EFFECT OF POSTURE ON INTRAGASTRIC DISTRIBUTION OF LIPID / AQUEOUS MEAL COMPONENTS AND THEIR GASTRIC EMPTYING.** P. Boulby, P. Gowland, V. Adams & R. C. Spiller. Depts. of Physics & Medicine, University of Nottingham, UK.

Previous scintigraphic studies have suggested that fat empties slower than the aqueous phase of mixed fat/water meals. Fat and water signals can be easily distinguished using the ultra fast MR imaging variant 'EPI'. We have used EPI to assess the intragastric distribution of oil and water with subjects lying either right side down (RSD) or right side up (RSU). **Methods:** Gastric emptying was assessed by serially measuring gastric volumes for up to 90 minutes. 8 healthy volunteers underwent 4 gastric emptying studies after consuming either test meals A or B in either RSD or RSU positions. The meals were 400 ml of beef consomme soup plus either 100 ml water (meal A, 46kcal), or 100 ml olive oil (meal B, 869kcal). **Results:** Gastric emptying of meal A was marginally faster with the Right Side Down, time to 50% gastric emptying T_{50} being 27±4 versus 33±4 min Right Side Up, $p<0.05$. Meal B emptied slower than A in the Right Side Down position, T50 being 43±2 min, $p<0.05$. By contrast gastric emptying was markedly prolonged after meal B in the RSU position with T_{50} in all cases >105 min, $p<0.01$. After ingestion of meal B oil was clearly observed layering above the water, filling the duodenal cap in the RSU position and the fundus in the RSD position. **Conclusions:** Gastric emptying of a low calorie meal is marginally faster when the pylorus is dependent. Adding fat inhibits gastric emptying, an effect which is much larger in the right side up position. We conclude that layering of fat influences gastric emptying which is strongly inhibited when fat fills the duodenum.

● **COLOCALIZATION OF NITRIC OXIDE SYNTHASE (NOS) AND N-METHYL-D-ASPARTATE (NMDA) RECEPTOR IN NEURONS CONSTITUTING THE CENTRAL PATTERN GENERATOR (CPG) FOR ESOPHAGEAL PERISTALSIS.** D. L. Broussard, X. Bao, X. Yu, S. M. Altschuler. Div. of Gastroenterology and Nutrition, Children's Hospital of Philadelphia. and University of Pennsylvania School of Medicine, Phila., PA.

Nitric Oxide (NO) production following NMDA receptor stimulation plays a prominent role in chemical synaptic signaling. As a readily diffusible gas, NO acts at both local and distant synaptic sites providing a mechanism to coordinate neuronal activity. We have independently identified NMDAR1 mRNA and NOS in neurons of the central subnucleus of the nucleus tractus solitarii (NTS_{cen}, interneurons constituting the CPG for esophageal peristalsis). The coexpression of NMDAR1 receptor protein and NOS within these neurons was investigated using transneuronal viral labeling with pseudorabies virus (PRV), immunohistochemistry (PRV and NMDA) and NADPH-d histochemistry (NOS). PRV was injected into the esophagus of adult rats and following a 60-65 hr survival, brainstem sections were processed for PRV and NMDAR1 immunofluorescence, and NADPH-d staining. PRV immunoreactivity (PRV-IR) was limited to the compact formation of the nucleus ambiguus (NA_c) and NTS_{cen}. NMDAR1 expression and NADPH-d staining were similar in control and PRV injected animals. The majority of PRV-IR neurons in the NTS_{cen} expressed NMDAR1 and were NADPH-d stained (triple labeled). In the NA_c, PRV-IR neurons expressed NMDAR1 but were not NADPH-d stained (double labeled). The colocalization of the NMDA receptor and NOS in CPG neurons provides the chemical substrates for integrating these neurons' activity throughout the NTS_{cen} and thus ensuring a precise sequence of esophageal motoneuronal activation in the NA_c. The absence of NMDAR1 and NADPH-d colocalization in the NA_c suggest motoneurons, in contrast to interneurons of the NTS_{cen}, utilize NMDA receptors for excitation without inducing NOS. Supported by the Robert Wood Johnson Foundation and NIH grant DK-44487.