was significantly correlated with the tachyarrhythmia and vomiting; also, the decrease of antral contraction was significantly associated with bradygastria and emetic symptoms (such as licking tongue or salivation) but not vomiting. 4) Gastric emptying of liquids was substantially delayed during vasopressin infusion (P<0.01, vs the corresponding period in saline control). Conclusion: Vasopressin induces both vomiting and nausea and each symptom has a specific motility pattern. This animal model for nausea and vomiting represents a good target for future pharmaceutical and device intervention.

Tu1811

Cortical & Physiological Responses to Visually Induced Motion Sickness

Adam D. Farmer, Vin Fei Ban, Gareth J. Sanger, Steven J. Coen, Paul Andrews, Qasim Aziz

INTRODUCTION - Nausea is a common and aversive experience, which negatively impacts on quality of life, adherence to treatment and is a cause for discontinuation of the development of novel compounds. Significant knowledge gaps remain in our understanding of the cortical and psychophysiological mechanisms involved in the genesis and maintenance of nausea. We aimed to develop and validate a readily administered a visually induced motion sickness (VIMS) stimulus to examine the psychophysiological changes induced by the stimulus and characterize the changes in cortical activity using functional magnetic resonance imaging (fMRI). METHODS - A 10-min video of motion and a control video of a still image were presented to 98 healthy volunteers (mean age 26 years, range 19-58 years, 53 male) in a randomized cross-over design. Validated questionnaires and visual analogue scales (VAS) were used for anxiety and nausea assessment. We monitored validated measures of autonomic and electrogastrographic activity at baseline and continuously thereafter. Subjects were stratified into quartiles based on nausea VAS scores with the upper and lower quartiles considered to be nausea sensitive and resistant respectively. Of these, 28 subjects of the 50 (mean age 25 years, range 20-49 years, 16 males, 11 nausea resistant) were exposed to the motion video during fMRI. RESULTS - All subjects completed the studies without vomiting. The motion video induced nausea in 57/98 subjects (57%) associated with elevation of median nausea VAS scores (2.0 (IRQ 1-3) vs. 1.0 (IRQ 1-1), p=0.003). Nausea sensitive subjects had lower normogastria:tachygastria (p=0.048), increased sympathetic (p=0.002) and decreased parasympathetic tone (p=0.03) during the motion video in comparison to the control video. The motion video resulted in heightened neuronal activity in the left and right cerebrum, temporal lobe, middle temporal gyrus and occipital lobe (p<0.004). Compared to nausea resistant subjects, the nausea sensitive group showed a paucity of activity in the left cerebrum, limbic areas and anterior cingulate cortex (p<0.001). CONCLUSION - This study provides evidence to validate the motion video as a VIMS stimulus. Additionally, it demonstrates the cortical and psychophysiological changes induced by VIMS. These changes are as a result of the activation of a broad central network, reflecting the multidimensional nature of nausea. Sensitivity to VIMS may therefore be as a consequence of failure of, rather than excessive, activation of cortical areas concerned with the interoceptive and affective aspects of nausea.

Tu1812

Uncertainty in Anticipation of Visceral Pain Is Modulated by the Autonomic Nervous System - A FMRI Study

Amandine Rubio, Chantal Delon-Martin, Sonia Pellissier, Nicolas Mathieu, Huynh Giao Ly, Jan F. Tack, Lukas Van Oudenhove, Bruno L. Bonaz

The brain responds by anticipation before the application of a painful stimulus. However, the differential role of uncertain versus certain anticipation of pain has never been studied. We aimed to analyze, in healthy volunteers, the brain regions implied in the uncertain versus certain anticipation of rectal pain and to examine the impact of heart rate variability (HRV) on the activity of these regions. Methods: The rectal distension threshold inducing a 70% discomfort was determined with a barostat in 15 healthy subjects. Six series of 12 fMRI trials were registered (MRI 3T Philips, 32 channels coil, spatial resolution 3x3x3mm3 and temporal resolution 3s). Each trial began with a period of cued anticipation, indicating that there would be ("!"), would maybe be ("?") or would not be ("0") a distension followed by the eventual distension and rating by each subject of experienced anxiety and discomfort. Images were analyzed with SPM8 software. Contrasts of uncertain versus certain anticipation were calculated for each subject, normalized into the MNI coordinate system using DARTEL registration method, and entered into a t-test random effect analysis. Concomitantly, electrocardiographic recordings were performed and the HRV components of interest were extracted. Since our fMRI data were acquired with a TR of 3s, only the Low Frequency (LF)-HRV band could be studied. Results: Uncertain anticipation of pain yielded 2 clusters of activation in the subgenual anterior cingulate cortex (sgACC) (p<0.001, Fig1). Certain anticipation of rectal pain led to the deactivation of brain regions composing the "pain signature network" (Wager et al, 2013). Brain regions with fMRI time courses correlating with LF-power fluctuation included the periaqueductal gray (PAG), the sgACC, right cerebellum and thalamus, bilateral hippocampus and occipital lobes (Fig 2). When the LF-component of the HRV was incorporated as a regressor in the fMRI analysis, uncertain anticipation produced stronger activation in the sgACC (cluster T-value increasing from 6.85 to 8.49). Discussion: The sgACC is associated with the affective component of pain, mood and motivation. The involvement of thalamo-corticoal regions in anticipatory processing of pain provides further evidence of dynamic connectivity along the entire neuroaxis in pain processing. These results are of great interest for pathologies involving viscerosensitivity. We plan to continue the study with Crohn's disease (CD) patients in remission since the unpredictability of flares in CD leads to marked impairment of quality of life in patients, generating great stress and anticipatory anxiety. Wager TD et al.An fMRI-based neurologic signature of physical pain. N Engl J Med. 2013;368:1388-97

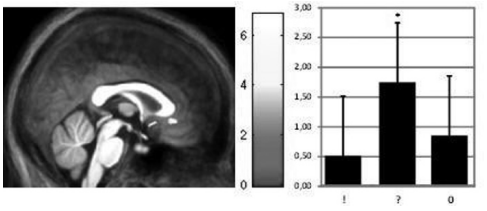

Fig1. Differential analysis of neural activation during cued uncertain vs (certain +safe) anticipation of rectal distension in all subjects. Activation of the sgACC (BA 34/32 and 25) and effect size depending on the type of anticipation (BA24/32) p<0.001.

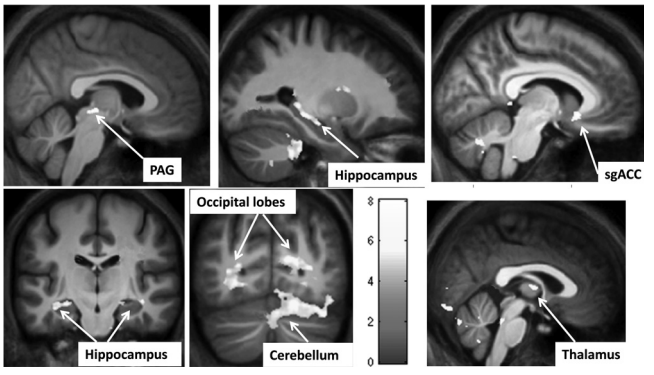

Fig2. Brain regions with fMRI time courses correlating with LF-power fluctuation included the periaqueductal gray (PAG), the sgACC, right cerebellum and thalamus, bilateral hippocampus and occipital lobes

Tu1813

Brain Fogginess, Gas, Bloating and Distension: A Link Between SIBO, Probiotics and Metabolic Acidosis

Abdul Rehman, Collier Badger, Neal Patel, Venugopalareddy Gangireddy, Satish S. Rao

Background: Bloating and distension are common and can be caused by small intestinal bacterial overgrowth (SIBO). But how these symptoms are associated with postprandial fatigue and brain fogginess in patients with intact gut is unclear. Our aim was to investigate whether brain fogginess, gas and bloating are due to d-lactic acidosis and SIBO. Methods: Consecutive patients presenting to our motility center with disabling and persistent symptoms of bloating and distention associated with brain fogginess, lack of concentration, near syncope, and muscle spasm for > 1 year were included in this study. Nine symptoms including abdominal pain, cramping, bloating, fullness, nausea, belching, indigestion, diarrhea and constipation were assessed at baseline and during the breath testing. Symptom severity was scored at baseline as frequency (0-3), intensity (0-3) and duration (0-3) and during breath test as 0 (absent) to 3 (severe). Additionally history of food fads, yogurt, probiotic consumption, over the counter medication and antibiotic use was collected. All patients were tested for SIBO with glucose breath test and duodenal aspirate and culture by passing 2mm Liguory catheter during endoscopy and culturing 3 ml fluid for aerobic, anaerobic and fungal cultures. Presence of metabolic acidosis was assessed with timed collection of serum or urine L-lactate and/or D-lactate in 5/6 patients after an oral carbohydrate (CHO) challenge. Results: Six patients (F/M=4/ 2, age range 38-71 years) were evaluated (Table 1). 5/6 had SIBO detected either by a positive breath test or by small intestinal culture. Brain fogginess was reproduced during breath test in all 6 patients. All patients had a history of yogurt consumption, and 2/6 consumed large amounts of homemade yogurt. All took regular probiotics and 5/6 had received antibiotics. All patients reported bloating and brain fogginess/spaciness and fatigue. 1/6 had explosive bloating. 1/6 had recurrent near syncopal episodes after CHO meals. Mean baseline symptom severity score of the nine symptoms is detailed in table 2. Discussion: We found a significant association between probiotics, SIBO, d-lactic acidosis, GI symptoms and brain fogginess/fatigue in all 6 patients. Antibiotics ameliorated key symptoms in 5/6 patients. These findings suggest that bacteria from probiotics and foods with active bacterial culture, although safe, in some may colonize the small bowel leading to SIBO and refractory symptoms. Furthermore lactobacilli tend to be resistant to antibiotics and cause d-lactic acidosis by fermenting carbohydrates in the food. The high lactate levels detected in our subjects explains their neuropsychological symptoms. With increasing use of probiotics and yogurt, this syndrome may be more widespread and merits further study.
Patient Demographics

Age	Sex	Yogurt/Probiotics	Bloating/Distention	Brain Fogginess	Fatigue	Breath tests Results	Small intestinal bacterial cultures	D-lactate	L-Lactate (serum)	Intervention	Response to Rx (% improvement)
61	M	+/+	++/++	+	+	-	+	serum -	+	Amoxicillin+clavilunate/Diet modification	80
71	F	+/+	++/+	++	+	+	-	serum -	-	Tinidazole/Diet modification	65
47	F	+/+	+/+	+	+	+	+	serum +	-	Amoxicillin+clavilunate/Diet modification	50
43	F	+/+	+/+	+	+	+	-	serum +	-	Amoxicillin+clavilunate+Tinidazole/Diet modification	60
38	F	+/+	+/+	++	+	+	-	serum +	n/a	Diet Modification	90
52	M	+/+	+/+	+	+	+	+	serum -	n/a	Levofloxacin Tinidazole/Diet Modification	90

Table 1
Mean baseline symptoms score of the study population

Symptoms	Pain	Cramping	Bloating	Fullness	Nausea	Belching	Indigestion	Diarrhea	Gas
Mean score	5.75	5.7	8.5	5.7	7.2	6.8	6	6.5	7.2

Table 2

Tu1814

Is Small Intestinal Bacterial Overgrowth Common in Chronic Pancreatitis?

Amelie Therrien, Simon Bouchard, Mickael Bouin

INTRODUCTION Chronic abdominal pain and steatorrhea are common complications of chronic pancreatitis (CP). Among possible multifactorial etiologies, small intestinal bacterial overgrowth (SIBO) is suspected. The prevalence and the factors promoting SIBO in CP patients are poorly known in the literature. AIM : To determine the prevalence of SIBO in patients with CP. METHODS : Prospective case-control study conducted at Centre Hospitalier de l'Université de Montréal (Quebec, Canada) from January to September 2013. Inclusion criterias: age 18 to 75 yo, clinical and radiological diagnosis of CP. Exclusion criterias: history of gastric, pancreatic or intestinal surgery, significant clinical gastroparesis. The presence of SIBO was detected using a standard breath test (ingestion of 10 g of lactulose followed by measurements of concentrations of hydrogen and methane in breath every 15 minutes for 3 hours). Positivity criterias validated in the literature and in force at CHUM are baseline H2> 20 ppm, peak of 20 ppm or two consecutive peaks of H2 or CH4 of 13 ppm during the first 90 minutes. Patients should not have taken antibiotics in the 30 days before and were asked to stop prokinetics and laxatives seven days before the test. Patients and controls were also asked to complete a standardized medical history questionnaire scoring the severity of different symptoms. The CP patients group was compared to a healthy control group. RESULTS: 31 patients (mean age 53.8 SD 14.1 years; 29% of female) and 40 controls (mean age 38.7 SD 12.1 years; 87% of female) were included. The prevalence of SIBO was significantly higher in patients than in controls (38.7% vs. 2.5%; $p < 0.01$). Women showed higher prevalence of SIBO than men (66.6 vs. 27.3%, $p = 0.05$). Among patients with CP, there were no differences between the subgroups with and without SIBO in terms of age, lifestyle, body mass index, etiology of the CP, use of opiates, pancreatic enzymes, PPI use or severity of symptoms. CONCLUSION : The prevalence of SIBO is high among patients with CP. We have shown no association between clinical features and the risk of SIBO except for gender. SIBO should be sought in all symptomatic patients with CP.

Tu1815

Acid-Stable Fungal Enzymes Improve Food Digestion and Nutrient Release in a Dynamic Human Stomach Model System

Duc Huy T. Do, Fanbin Kong, Chris Penet, Thomas Laaman, Debbie Winetzky, Kelly Gregory

Background: Patients suffering from pancreatic insufficiency and other ailments including surgeries or injuries that affect the body's normal production of digestive enzymes are conventionally treated with encapsulated animal derived pancreatic enzymes. This approach has many issues in terms of solubility, functionality and efficiency when applied into the digestive system at lower pH's typically found in the upper GI. The use of fungal enzymes can be used to improve digestion and thus increase nutrient availability for these patients. These enzymes are typically found as supplements that can withstand the acidic pH level of the stomach can help in breaking larger carbohydrates, fats, and proteins into manageable molecules for the small intestine to be absorbed. An enzyme cocktail containing 4 acid stable fungal enzymes were tested in an in vitro stomach system to examine the efficiency in assisting digestion. Methods: Two enzyme cocktails containing high and low concentration of the enzyme mixtures (referred to High Activity Blend and Low Activity Blend, respectively), were tested in the dynamic stomach model. A prescription pancreatic enzyme mixture Creon (commercially available) was used as control. The dynamic stomach model simulates peristaltic movement of stomach walls, the continuous secretion of stomach acid and enzymes, and stomach emptying. The enzymes blends were mixed into customer-made food matrix containing canola oil, starch, and tuna. The emptied digesta (mixture of stomach contents) were collected and analyzed for free amino nitrogen, glucose, and glycerol, as an indicator of breakdown of proteins, carbohydrates, and fats. Results: Both the High Activity and Low Activity Enzyme blends were able to outperform the control by providing more breakdown of protein, lipids and carbohydrates, and the High Activity Blend showed the highest efficiency. The content of free amino nitrogen in the digesta increased in the first 1 hour, and then continuously decreased due to stomach emptying that continuously removed the enzyme and the digestive products (Fig. 1). The free amino Nitrogen reached 570 mg/L at 60 minutes for High Enzyme Blend, compared to 410 mg/L and 370 mg/L for the Low Enzyme Blend and control (Fig. 1). Similar results were observed for glucose and glycerol: High Activity Enzyme blend broke down the substrate and generated approximately 4 times the amount of glucose, and 4 times the amount of glycerol compared to the control. Conclusion: Supplements with acid stable fungal enzymes can help break down larger molecules into more manageable molecules for the body to absorb. The dynamic stomach model is suitable to exhibit the digestion process and the change of the digestive products.

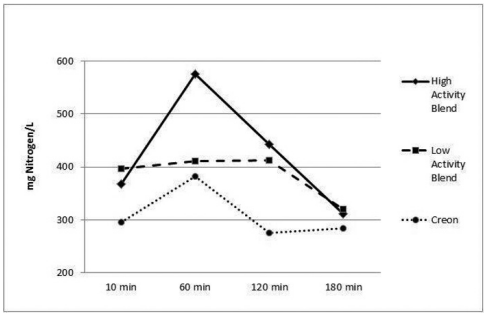

Figure 1: Content of free amino nitrogen during simulated gastric digestion with three enzyme mixtures.

Tu1816

Association of ADH2, ADH3, CYP2E1 and CAT Gene Polymorphisms in Patients With Pancreatic Cancer

Rajendra P. Ola, Satya Vati Rana, Rajesh Gupta, Surinder S. Rana, Deepak K. Bhasin

Background: Pancreatic cancer is a heterogeneous disease. Alcoholism is the most common cause of pancreatic cancer, worldwide. Susceptibility to organ damage induced by alcohol may be related to genetic polymorphisms in alcohol metabolizing enzyme genes. Alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH) are principal enzymes responsible for metabolism of ethanol. Alcohol is also metabolized in extra hepatic tissues, by the enzymes cytochrome P450 (CYP2E1) and catalase (CAT). CYP2E1 activity is expressed in the liver and pancreas, where it is induced by chronic alcohol consumption. Functional polymorphisms of ADH2, ADH3, ALDH2, CYP2E1 and CAT genes occur among racial populations. AIM: To compare the genotype frequencies of ADH2, ADH3, ALDH2, CYP2E1 and CAT genes in patients of pancreatic cancer with healthy subjects from North India. Materials and Methods: Genotyping analysis of ADH2, ADH3, ALDH2, CYP2E1 and CAT genes were conducted in 65 patients with pancreatic cancer (PC) and 100 healthy volunteers by the PCR-RFLP assay. RESULTS: Polymorphic alleles distribution in PC was 69.2% ADH2*1/1, 61.8% ADH3*1/1, 80% CYP2E1*C1/C1 and 27.7% CAT*T/T while in controls, 48% ADH2*1/1, 42.7% ADH3*1/1, 66% CYP2E1*C1/C1, and 16.7% CAT*T/T. Polymorphic alleles of ADH2*1/1, ADH3*1/1, CAT*T/T genotype frequency were significantly higher ($p < 0.05$) in patients with PC as compared to controls. The genotype CYP2E1*C1/C1 had no significant association with pancreatic cancer. CONCLUSIONS: ADH2*1/1, ADH3*1/1, CAT*T/T alleles were significantly higher in patients with pancreatic cancer from North India.

Tu1817

Frequency of SPINK1 N34S Mutation in Acute and Recurrent Acute Pancreatitis

Praveer Rai, Anjali Sharma, Ankur Gupta, Rakesh Aggarwal

Introduction: Several studies have reported association of N34S mutation in SPINK1 gene with chronic pancreatitis; however the data on its relationship with acute pancreatitis (AP) and recurrent acute pancreatitis (RAP) are limited. Methods: We studied 183 unrelated patients with AP and RAP and 168 healthy controls for N34S variant in SPINK1 gene using sequencing of genomic DNA. Results: SPINK1 N34S mutation was found in 4 of 168 (2.4%; all heterozygotes) controls and 22 of 183 (12.0%; including one homozygote) patients with AP ($p= 0.006$). On subgroup analysis, seven of 70 (10.0%) patients with gallstone-related AP, 8 of 59 (13.6%; including one homozygote) patients with idiopathic AP, and 6 of 44 (14.6%) patients with alcohol-related AP had the N34S mutation ($p=0.027$, 0.002 and 0.006, respectively, compared to controls). Frequency of this mutation was similar in patients with one episode of AP and those with recurrent AP (12% each). The first attack of AP occurred earlier in patients with N34S than in those without it (mean + SD age: 32±9.7 versus 39.1±13.4 years; $p=0.004$). No patient had any other mutation in the exon 3 of the SPINK1 gene, whereas one control had a heterozygous P55S mutation. Conclusions: N34S mutation in SPINK1 gene was found more frequently found in patients with AP in the Indian population, irrespective of disease etiology and whether the disease was recurrent or not, and was associated with disease onset at an earlier age. These findings suggest that N34S mutation lowers the threshold for occurrence of AP irrespective of the causative insult.

Tu1818

Similarities and Differences in Admission Characteristics and Short-Term Outcomes Among Individuals With Acute Pancreatitis (AP) of Differing Races Admitted to an Urban Medical Center

Ji Young Bang, Timothy D. Imler, Gregory A. Cote

Background: Recent data suggest differing mortality trends among white and black adults in the U.S. with pancreatic cancer. For individuals admitted with acute pancreatitis (AP), there is a paucity of studies comparing admission characteristics and short-term outcomes among different races. We examined these factors, with a particular emphasis on mortality, length of stay, and use of same-stay ERCP and cholecystectomy (CCY). Methods: We studied a cohort of patients ≥18 years of age admitted with AP (defined using International Classification of Diseases, 9th Revision code 577.0) at a single, urban medical center between 2002-2012. Patients were classified by race (White, Black, Hispanic/Other) according to self-report. Across races, demographics, admission characteristics (including relevant laboratories and Systemic Inflammatory Response (SIRS) criteria), use of same-stay ERCP and CCY, and outcomes (length of stay and inpatient mortality) were compared. Results: During the study period, 2150 patients were admitted with AP (median age 47 years (interquartile