in normal and constipated rats. Daily oral capromorelin was also effective in causing bowel emptying.

doi:10.1016/j.autneu.2015.07.027

P2.13
Electrical vagus nerve stimulation as an innovative treatment in inflammatory bowel diseases

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The vagal cholinergic anti-inflammatory pathway involves the inhibition of pro-inflammatory cytokines release. Our previous studies revealed firstly, a blunted vagus nerve activity in Crohn's Disease (CD) patients and secondly, an improvement of colitis in rats after electrical vagus nerve stimulation (eVNS). Consequently, a clinical eVNS study was performed in CD patients (Clinical Trials.gov NCT01569503). The main goal was to evaluate the safety and efficacy of this innovative treatment. Six CD patients under intestinal active inflammation were included and equipped with a vagal nerve stimulation device (Cyberonics Inc.). Stimulation parameters were 10 Hz, 500 μs, 0,5 mA, 30 s ON, 5 min OFF. Three main types of markers were measured during a one-year follow-up: clinical (Crohn's disease activity index –CDAI-), biological (C-reactive protein-CRP-) and autonomic (heart rate variability-HRV-). Currently, the study is still running and only the six first month of follow-up are presented herein. Four patients have an improvement of 1) their clinical state marked by a decrease in CDAI, 2) their parasympathetic tone (HRV) which returns to an homeostatic level, 3) their biological state by a decrease in CRP. No adverse effect of eVNS was observed. In conclusion, these results show for the first time that eVNS in CD patients is safe and well tolerated. Moreover, long-term eVNS induces an effective improvement over the six first month and further next results will show us if this improvement is maintained over the one year follow-up. eVNS, devoided of problem of compliance, could be of interest as an alternative to classical pharmacological therapies.

doi:10.1016/j.autneu.2015.07.028

P2.14
Oral ingestion of a 5-HT4 receptor agonist evokes a CNS-ENS mediated gastro-colonic reflex involving High Amplitude Propulsive Contractions (HAPCs) in the human colon within 5 minutes

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Assessment of neurogenic colon motor functions is a challenge since the colon may not show activity for long periods of time. Appropriate stimuli are required during assessment in order to evaluate myogenic and neurogenic functions or abnormalities. We performed high-resolution manometry using 36 solid-state sensors, 1 cm apart in 15 patients with chronic constipation or IBS-D and volunteers. Oral prucalopride is rapidly absorbed independent of food intake and maximal bioavailability is reached within 1-3 hours (1). Oral prucalopride (2 mg) had a biphasic effect. A first excitation of the colon musculature was seen within the first 20 min, and a second excitation was seen after 40 – 90 min. The first excitation produced an HAPC in 4 of 17 subjects studied at 4.1 ± 1.1 min after ingestion; or an increase in haustral boundary contractions (HC) and/or simultaneous contractions (SC) in 7/17 was observed at 7.8 ± 3.1 min. The second excitation consisted of HAPCs in 4 out of 15 studied, at 58.0 ± 4.8 min, or HC and SCs in 11/15 at 45 ± 10 min. In all 17 subjects, baseline HAPCs were never observed and in only 1 subject an HAPC occurred after a meal. We infer that prucalopride affects 5-HT4 receptors on gastric or duodenal enterochromaffin cells (2) to elicit a CNS-ENS mediated gastro-colonic reflex in addition to its prokinetic effect observed after full bioavailability is reached. Prucalopride therefore may be useful as a test substance to evaluate the ability to generate 5-HT4 mediated neurogenic motor patterns in the human colon. Supported by grants from the National Natural Science Foundation of China and the Canadian Institutes of Health Research.

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doi:10.1016/j.autneu.2015.07.029

P3 Thermoregulation/Hidrosis

P3.1
Sympathetic tonus modify endothelial dependent vasodilation in finger pulp of healthy subjects

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The activity of the sympathetic nervous system (SNS) is increased in Raynaud´s phenomenon (1) and cooling elicits attacks. We studied the impact of SNS on endothelium dependent vasodilation of the arterioles and the arteriovenous anastomoses (AVA) in hands of healthy subjects (2). Thirteen subjects were exposed to Thermoneutral (29 °C) and Cold (22 °C) room temperature on separate days. Simultaneous bilateral continuous measurements of laser Doppler flux were obtained from AVA skin (finger pulp) and arteriole skin (dorsal wrist). After baseline measurements, flow mediated dilatation (FMD) was induced by shear stress (release of a 4-min suprasystolic pressure cuff applied to the right forearm). Normalized FMD peak (median, and 95% confidence interval) after cuff deflation relative to baseline (baseline value = 1.0) was calculated. In Thermoneutral, the baseline AVA flux (median 236 au) showed synchronous fluctuations in both hands not apparent in baseline arteriolar flux (median 23 au). In Cold, both baseline AVA flux (145 au) and arteriolar flux (15 au) showed minimal or no fluctuations. The FMD peak in AVA was higher in Cold (3.1 (2.5, 4.5)) compared to Thermoneutral (1.4 (1.1, 1.6), $p = 0.002$). The FMD peak in the arterioles in Cold (3.5 (2.3, 4.0)) and Thermoneutral (2.4 (1.7, 2.8) were not significantly different ($p = 0.16$). High SNS activity to the AVAs during cooling more than doubled the influence of endothelium dependent vasodilatation on the finger pulp flux compared to thermoneutral condition. Impaired endothelial vasodilation may explain occurrence of ischemic digital ulcers during attacks in secondary, but not in primary Raynaud's phenomenon.

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