

PTU-128 A NOVEL ASSOCIATION BETWEEN COMT GENE POLYMORPHISMS AND RISK OF SYMPTOMATIC DYSPHAGIA IN THE ELDERLY

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Introduction Genetic variants of the enzyme Catechol-O-Methyl Transferase (COMT) have been associated with age related degeneration and changes in dopamine function. Further, COMT gene polymorphisms have been found to interact with other genes in affecting levels of brain plasticity. We hypothesised, given the link with dopamine and brain function, interactions between polymorphisms of the COMT gene would predict dysphagia symptoms in an elderly population.

Methods 800 members of a genetically well characterised community dwelling elderly cohort received the Sydney oro-pharyngeal dysphagia questionnaire (1) via mail. A score of 180 or more was indicative of significant dysphagia. Saliva samples were assessed for COMT polymorphism carrier status. The carrier status of each polymorphism was investigated for association with dysphagia symptoms. Logistic regression analyses were performed in SPSS to investigate whether any of the polymorphisms under consideration were predictive of dysphagia after adjusting for age and gender, in addition to interaction effects between polymorphisms.

Results 638 subjects (80%) returned the questionnaire, 150 were men and 488 women and the mean age was 81.2 years. Saliva samples were then analysed for 540 of these subjects and 82 (15%) of these had significant dysphagia with scores ≥ 180 . COMT polymorphisms *rs165599* and *rs10835211* were found to be associated with dysphagia symptoms with a significant interaction between the two ($p = 0.018$). The effect of each of these two polymorphisms varied according to the carrier status of the other. In the case of *rs10835211*, the effect of heterozygosity was protective or harmful dependent on the respective status of *rs165599* (Table 1), with *rs165599* homozygosity producing a $> 400\%$ increased risk of dysphagia.

Abstract PTU-128 Table 1 Predictors of dysphagia symptoms

Predictor	Adjusted OR	95% CI
<i>rs165599</i>	0.86	0.39- 1.84
<i>rs10835211</i>	4.35	1.66- 11.41
Interaction	0.21	0.06- 0.77

Conclusion We have found a novel relationship between self-reported symptoms of dysphagia and COMT status of polymorphisms *rs165599* and *rs10835211*. Depending on their carrier status, the odds of having dysphagia can either be increased or decreased. These results also demonstrate the importance of genetic factors in age related problems, such as dysphagia.

Disclosure of Interest None Declared

REFERENCE

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PTU-129 ANAL EVOKED POTENTIALS AT 'TWITCH' THRESHOLD: A NEW METHOD FOR EXPLORATION OF ANAL SENSORY FUNCTION

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Introduction Faecal incontinence can be associated with impaired anal sensitivity. Anal evoked potentials (EPs) have previously been used to quantify anal sensory function; however the traditional technique of stimulating at a percentage of pain threshold may result in poorly reproducible results with significant inter-individual variability. The aim of this study was to develop a reliable and reproducible method of recording anal EPs, and to define waveform characteristics in healthy volunteers.

Methods Twenty eight healthy volunteers (21 F, median age 34 [range 21–74]) without bowel dysfunction were recruited for the study. Anal EPs were recorded in response to stimulation (using a bipolar electrode) 1cm from the anal verge. In contrast to previous studies, stimulation intensity was delivered at motor threshold (determined by visualisation of an anal 'twitch'). Four sets of 50 stimuli (0.2 Hz frequency, 0.2 ms pulse duration) were given with 5-minute intervals between sets to reduce habituation. A repeat study was performed in 7 volunteers after a minimum interval of 2 weeks. Recordings were taken between channels Cz-A1 and Cz'-Fz (International 10–20 system) in accordance with previously published literature. Runs were averaged and latencies for EP responses were defined, analysed and compared.

Results Motor threshold stimulation (median 20, range 10–36 mA) was well tolerated in all volunteers and resulted in reproducible polyphasic waveforms. The first negative peak (N1) was clearly identifiable on all traces. In the Cz'-Fz channel, the latency to N1 was 130 ± 20 ms (coefficient of variation [COV] = 15%). This was less variable than N1 in Cz-A1 (153 ± 34 ms; COV = 22%) and much less than published previously (COV of N1 = 39%; Remes-Troche *et al. Neurogastroenterol Motil* 2011). Analysis of repeat studies demonstrated that latencies in channel Cz'-Fz were the most reproducible (ICC of N1 latency = 0.95 [very strong agreement]).

Conclusion Electrical stimulation at motor threshold and recording of evoked potentials from channel Cz'-Fz is a reliable and reproducible method for examination of anal sensory function. Latency to N1 is the most consistent waveform component and is highly reproducible. The technique of stimulation at 'twitch' threshold appears to reduce inter-subject variability and may allow application to further explore both the pathophysiology of anal dysfunction and the effect of treatments aimed at modulating anal neuronal function.

Disclosure of Interest None Declared

REFERENCE

- Remes-Troche JM, Tantiphlachiva K, Attaluri A, *et al.* A bi-directional assessment of the human brain-anorectal axis. *Neurogastroenterol Motil* 2011; **23**: 240–248, e117–248

PTU-130 DOES CHRONIC COUGH PROVOKE INCREASED GASTRO-ESOPHAGEAL REFLUX?

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Introduction Chronic cough and GERD are very common and prevalent diseases. It is known that GERD is one of the three most common causes of chronic cough. During the last years, new methods have been introduced to study the temporal and causal association between reflux and cough. pH-impedance monitoring has been proposed as the most sensitive method for detection of acid and non acid reflux whereas either manometric or acoustic methods have been used for objective detection of cough. During these studies, a sequence of association of "reflux-cough" has been used

to establish a positive diagnosis. The sequence cough-reflux has also been described but controversy still exist about its prevalence and clinical relevance. One potential factor for such controversy could be due to different methodology for cough detection. The **aim** of this study was to assess the contribution of cough to pathologic GER in patients with chronic cough and increased esophageal acid exposure.

Methods Simultaneous 24h ambulatory reflux and cough monitoring was performed in 17 patients with suspected reflux-related chronic cough. Reflux episodes were detected by pH-impedance monitoring and coughs by a) manometric detection and b) acoustic detection (independent listening of complete 24hs sound recordings). Manometric cough detection was performed with a two-channel pressure catheter with sensors in the oesophagus and stomach. Cough was manually declared when simultaneous abdomino-thoracic pressure bursts occurred of at least 2 peaks within 3 seconds. Acoustic detection was performed using 3 sound surface sensors. Cough events were identified and inserted into the reflux tracing. We measured total esophageal acid exposure and bolus exposure (by impedance). We calculated the time of acid exposure and bolus exposure after manometrically and acoustic detected cough events.

Results 6/17 patients had pathological esophageal acid exposure. In these patients the total number of reflux events/24hs was 38 (29–70). From that total number, 7.4% (0–25) reflux episodes occurred within 2 minutes after a cough episodes. Total acid exposure was $9.7\% \pm 4.7$. From the acid exposure, 3.5% (0–8)% occurred after cough detected by manometry or audio. The median total bolus exposure was $2.1 \pm 0.6\%$. From total bolus exposure, 6.3% (0–20) occurred after manometric cough detection and 6.8% (0–50) after acoustic detected cough. Only 1/6 patients had a significant increase in acid and bolus exposure after cough.

Conclusion In patients with chronic cough and pathological acid GER, cough was followed by reflux in a minority of cases regardless of the method for cough detection. In only 1/6 patients the sequence cough-reflux could be considered as causal of pathological GER.

Disclosure of Interest None Declared

PTU-131 OESOPHAGEAL THERMAL SENSITIVITY AND MUCOSAL INTEGRITY IN HEALTHY SUBJECTS. A STUDY USING A NOVEL Peltier-BASED HEATING DEVICE AND IMPEDANCE

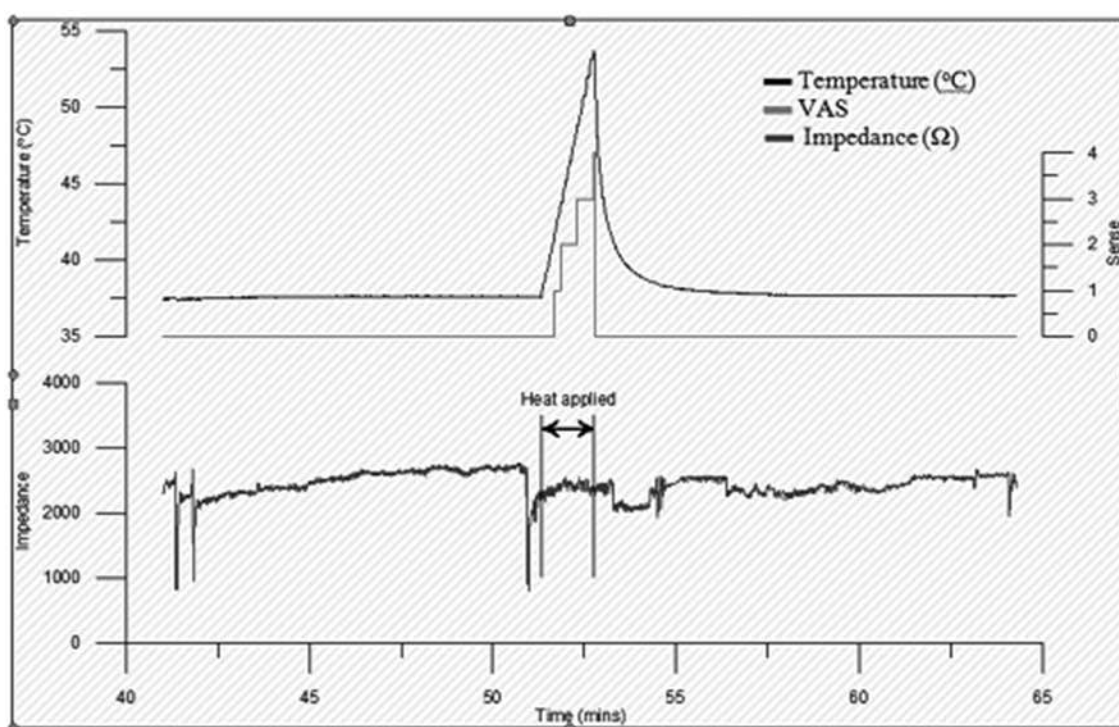
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Introduction Investigation of oesophageal sensitivity might help better improve phenotyping of patients with GERD, functional heartburn and non-obstructive dysphagia. Studies on oesophageal thermal sensitivity have used balloon techniques with circulating water. This lacks linear control of heating, has relative heat loss, and provokes mechanical stimulation by the distended balloon. Oesophageal mucosal integrity is important in symptoms perception and can be studied using impedance “in vivo”. We developed a catheter device incorporating a “thermal stimulator” using Peltier heating technology and impedance electrodes to assess mucosal contact and integrity. We **aimed** to investigate oesophageal heat sensation/pain thresholds and their relationship with mucosal integrity in healthy human subjects.

Methods 21 healthy volunteers underwent thermal stimulation using an oesophageal catheter with a 7 mm electronic Peltier heater, to deliver a ramp heating protocol up to 60°C at 5 and 15 cm above LOS. Symptoms were recorded by computerised Visual Analogue Score (VAS). The delivered temperature at Pain Detection Threshold (PDT), time to PDT was measured and the area under the heating curve (AUC) was calculated. Oesophageal impedance was assessed over 10 minutes pre (basal), during and post heating in the distal and proximal oesophagus. The protocol was repeated after 2 weeks to assess reproducibility.

Results Temperature at PDT showed a very low SD in the distal and proximal oesophagus and Bland-Altman Tests showed good reproducibility (−0.1905 95% CI −1.4132 to 1.0327). There were no significant differences in thermal sensitivity parameters between distal and proximal oesophagus. Due to the low inter-individual



Abstract PTU-131 Figure