on Levodopa (Group B) showed significant decrease (inhibition) in brainstem reflexes amplitude after Levodopa.

Conclusion Different patterns of cortical and brainstem activity, reflecting different mechanisms of compensation with Levodopa intake, can differentiate dysphagic PD groups. Moreover, physiology was negatively affected by L-dopa in groups with inhibition of brainstem reflexes. Our novel brain stimulation data demonstrate the dysphagia in PD patients is associated with altered cortical and brainstem activity, modulated by L-dopa differentially across the PD groups, providing the platform for research on rehabilitation for dysphagia in PD.

Disclosure of Interest None Declared

OC-035 MECHANISM OF LACTOSE INTOLERANCE IN IRRITABLE BOWEL SYNDROME: ROLE OF ANXIETY, MUCOSAL IMMUNITY AND VISCERAL HYPERSENSITIVITY

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Introduction Many patients, especially those with Irritable Bowel Syndrome (IBS), report food intolerance; however the mechanism underlying these “functional digestive symptoms” is unknown. We assessed the role of psychological factors, mucosal immune activation and visceral sensitivity on the development of lactose intolerance (LI) after ingestion of 20g lactose in IBS patients and healthy controls (HCs) with lactase deficiency: a validated, clinical experimental model of intolerance to poorly absorbed, fermentable foods (Yang *et al* Clin Gastro Hep 2013 in publication).

Methods IBS-D patients meeting Rome III criteria (n = 277) and age/sex matched HCs (n = 64) underwent a 20g lactose hydrogen breath test (LHBT) with measurement of hydrogen production, abdominal distention, and LI symptoms. Hospital Anxiety and Depression Score assessed psychologic state. Barostat measured rectal sensitivity. Additionally, 55 IBS-D patients and 18 HCs completed colonoscopy with colon and terminal ileum (TI) biopsies for quantification of mast cells (MCs), T lymphocytes, and enterochromaffin cells (ECC).

Results Hydrogen production and distention were similar in IBS patients and HCs during LHBT; however LI symptoms were more frequent in IBS (54% vs. 28%, $P < 0.001$), including bloating (39% vs. 14%, $P < 0.001$), borborygmi (39% vs. 22%, $P = 0.010$), pain (31% vs. 11%, $P = 0.001$) and diarrhoea (29% vs. 9%, $P = 0.001$). IBS patients were more anxious ($p < 0.001$) and had higher rectal sensitivity than HCs ($P = 0.001$). Multivariate analysis indicated that hydrogen production increased the likelihood of bloating (OR2.2 (95%CI 1.1–4.4), $P = 0.028$) and borborygmi (OR12.4 (3.3–45.8), $P < 0.001$), but not objective distention ($P = 0.673$). Visceral hypersensitivity also associated with bloating (OR6.6 (1.7–25.0), $P = 0.005$) and total symptom score (OR3.7 (1.3–10.9, $P = 0.014$). A planned subanalysis showed that, compared to IBS patients with no symptoms, those with LI were more anxious ($p = 0.045$) and more likely to have visceral hypersensitivity ($p < 0.001$).

In those that had colonoscopy, IBS patients with LI (25/55 (45%)) had increased MCs ($p < 0.006$), T-cells and ECC (both $p < 0.05$) in proximal colonic and TI mucosa compared to patients without LI and HCs. Multivariate analysis indicated that total LI symptom score was associated with anxiety ($r = 0.519$, $P < 0.001$), MCs in terminal ileum ($r = 0.650$, $P < 0.001$) and visceral sensitivity ($r = 0.629$, $P < 0.001$).

Conclusion Gas production and sensitivity to luminal distension both contribute to digestive symptoms after lactose ingestion in

patients with lactase deficiency. IBS-D patients with LI are characterised by anxiety, evidence of mucosal immune activation and visceral hypersensitivity.

Disclosure of Interest None Declared

OC-036 NEURONAVIGATED REPETITIVE CEREBELLAR STIMULATION PRODUCES LONG-LASTING ACTIVATION OF HUMAN CORTICAL SWALLOWING PROJECTIONS

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Introduction Animal studies, human brain imaging and more recently Transcranial Magnetic Stimulation (TMS) suggest a role for the cerebellum in human swallowing. Moreover, paired-pulse cerebellar-cortical TMS delivered in rapid succession (50–200 ms intervals) facilitates pharyngeal motor cortex excitability. We therefore hypothesised that high-frequency (5–20 Hz) repetitive TMS (rTMS) of the cerebellum could modulate pharyngeal motor cortex excitability producing long-lasting changes that may prove to be therapeutically useful for dysphagia after stroke.

Methods In 17 healthy adults (6 female, age range 18–61 yrs), anatomical MR brain scans were acquired. Thereafter participants were intubated with an intraluminal catheter to record pharyngeal electromyography and underwent TMS cortical mapping with neuronavigation to co-localise pharyngeal motor representation bilaterally, hand motor cortex and the cerebellar site which evoked the largest pharyngeal motor response. Subjects were then randomised to receive one of 5 neuronavigated cerebellar rTMS interventions (Sham, 1 Hz, 5 Hz, 10 Hz and 20 Hz, at least 1 week apart) to the cerebellar site evoking the largest baseline pharyngeal responses to single-pulse cerebellar TMS. Bihemispheric pharyngeal cortical excitability (ipsilateral and contralateral cortex to cerebellum site) was measured at baseline and for up to one hour post cerebellar rTMS intervention. Abductor pollicis brevis (APB) recordings were used as control. Interventional data were compared to sham using repeated measures ANOVA.

Results Cerebellar rTMS was tolerated well and delivered at an average intensity of 55% of stimulator output. Compared to Sham, 10 Hz cerebellar rTMS increased pharyngeal cortical excitability ($F(1.16) = 8.3$, $*p = 0.01$), with maximal size and durational effects seen primarily in the contralateral pharyngeal cortex (+72%, $**p = 0.02$, Figure 1). By contrast, 1 Hz ($F(1.16) = 0.3$, $p = 0.60$), 5 Hz ($F(1.16) = 0.5$, $p = 0.48$), and 20 Hz rTMS ($F(1.16) = 1.3$, $p = 0.27$) cerebellar conditioning did not significantly alter pharyngeal excitability compared to Sham. APB responses were not significantly different to sham after any intervention.

Abstract OC-036 Figure 1 Effects of 10 Hz Cerebellar rTMS on pharyngeal cortical excitability.

Conclusion Our data show for the first time that high-frequency (10Hz) cerebellar stimulation can produce long-lasting increases in human pharyngeal motor cortex excitability, with larger and longer-lasting effects of the intervention primarily seen in the contralateral projection. Hence 10Hz cerebellar rTMS may play a therapeutic role in the treatment of dysphagia after hemispheric stroke.

Disclosure of Interest None Declared

OC-037 DOES LEARNING OF ILLNESS BEHAVIOUR IN CHILDHOOD INFLUENCE THE DEVELOPMENT OF IRRITABLE BOWEL SYNDROME?

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Introduction We have previously shown that a twin with IBS was more likely to have a mother with IBS than a co-twin with IBS. This may be because learned illness behaviour in childhood is as important as genetic factors in the aetiology of IBS. We have examined the association of learned illness behaviour with IBS in our twin cohort.

Methods 6552 unselected twins were asked to complete a validated questionnaire including the social learning of illness scale. IBS was categorised by Rome III criteria into 3 groups: extended criteria IBS, limited criteria IBS (symptoms more than once a week) and a medical IBS diagnosis.

Results 4128 subjects replied (63%). 3349 were evaluable (91% female, median age 62 (IQR 53–69)). Univariate analysis revealed that only a medical diagnosis of IBS was associated with an increasing score on the social learning of illness scale (Table 1). Other factors associated with all three sub-types of IBS were increasing psychosomatic score, anxiety, female gender, younger age and having a parent with IBS. Social learning of illness behaviour and all these factors were independently associated with a medical diagnosis of IBS. Modelling of illness behaviour (OR 1.06, 95% CI 1.01–1.12, $p = 0.04$) and reinforcement of the sick role (1.1, 95% CI 1.01–1.2, $p = 0.04$) were found to be significant predictors of a medical diagnosis of IBS. However, encouragement of the sick role was not associated with a medical diagnosis of IBS.

Conclusion A higher score for social learning of illness behaviour was associated with a medical diagnosis of IBS. This was independent of other risk factors for IBS. In our twin cohort, the aspects of learned illness behaviour which influenced the development of IBS were reinforcement of the sick role and modelling of illness behaviour. Social learning of illness behaviour did not appear to influence IBS as defined by Rome III criteria when a medical diagnosis was not made, suggesting that it drives health care seeking behaviour rather than necessarily being an aetiological factor for IBS.

Disclosure of Interest None Declared

Pancreatic free papers

OC-038 SPECIFIC MICRORNA MARKERS ARE IDENTIFIED IN BILE IN PANCREATIC DUCTAL ADENOCARCINOMA

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Introduction MicroRNAs (miRNAs) are short, non-coding RNAs with a key role in post-transcriptional regulation, and regulate multiple pathways of tumorigenesis. Expression profiling of malignant cell lines, fresh and formalin-fixed tumour have identified potential miRNA signatures for pancreatic ductal adenocarcinoma (PDAC), and RNA deep sequencing has demonstrated that miRNAs can be quantified from bile, in biliary tract cancers¹. Here, we report the first study of biliary miRNAs in PDAC.

Methods 3 target miRNAs known to be overexpressed in PDAC were selected. Bile was collected at endoscopic retrograde cholangiopancreatography (ERCP) from patients with PDAC ($n = 10$) or gallstones ($n = 8$; used as a benign control). Bile was prepared as described¹ and total RNA isolated using TRIzol (Invitrogen, Paisley, UK). Quantitative real-time reverse-transcription polymerase chain reaction (RT-qPCR) was performed using Taqman mature miRNA primers and probes (Applied Biosystems, Cheshire, UK). Expression of oncomiR-21, miR-155 and miR-106a was measured. Cycle passing threshold (Ct) was recorded and normalised to RNU6B expression. Relative expression was calculated as $2^{Ct_{miRNA} - Ct_{RNU6B}}$. PCR reactions were carried out in duplicate.

Results miR-106a and oncomiR-21 were both highly expressed in the bile of patients with PDAC, compared to those with gallstones. miR-155 was not significantly upregulated in PDAC bile. Using miR-106a (cut-off level > 8.02), we discriminated PDAC from benign disease with a sensitivity and specificity of 80% [95% CI 44–98] and 100% [95% CI 63–100], respectively with an area under the curve (AUC) value of 0.88. OncomiR-21 was also upregulated in bile, but was not as reliable in discriminating diagnosis.

Conclusion This study demonstrates that bile miRNAs are well-suited analytes for the development of sensitive and specific tests in PDAC. Although tumour breach of the biliary epithelium was not always suspected in our cohort from clinical investigations, malignancy-specific miRNAs were found intraluminally. Of the 3 miRNAs tested, ROC analysis identified miR-106a as the best potential PDAC biomarker, with reliable diagnostic specificity and sensitivity. However, further study may also identify miRNAs that also discriminate prognoses and response to therapy, guiding individualised treatment.

Disclosure of Interest None Declared

REFERENCE

- Shigehara K, Yokomuro S, Ishibashi O, *et al*. Real-time PCR-based analysis of the human bile microRNAome identifies miR-9 as a potential diagnostic biomarker for biliary tract cancer. *PLoS one*. 2011; 6(8):e23584.

Abstract OC-037 Table 1 Univariate analysis of factors associated with IBS

VARIABLE	ROMEIII EXTENDED CRITERIA IBS	ROME III LIMITED CRITERIA IBS	MEDICAL DIAGNOSIS IBS
Social Learning of Illness Behaviour Scale	0.89 (0.66–1.21, $p = 0.47$)	1.00 (0.99–1.01, $p = 0.5$)	1.15 (1.13–1.17, $p < 0.01$)
Psychosomatic score	1.19 (1.17–1.21, $p < 0.001$)	1.21 (1.19–1.24, $p < 0.001$)	1.15 (1.13–1.17, $p < 0.001$)
Anxiety	1.75 (1.47–2.09, $p < 0.001$)	1.54 (1.19–1.98, $p = 0.001$)	1.84 (1.40–2.42, $p < 0.001$)
Female gender	2.16 (1.54–3.03, $p < 0.001$)	2.94 (1.48–5.85, $p = 0.002$)	2.19 (1.18–4.05, $p < 0.001$)
Age	0.99 (0.98–0.99, $p = 0.001$)	1.03 (1.03–1.04, $p < 0.001$)	1.11 (1.10–1.12, $p < 0.001$)
Parent IBS	2.48 (2.00–3.08, $p < 0.001$)	1.81 (1.35–2.43, $p < 0.001$)	2.72 (2.15–3.44, $p < 0.001$)