

overweight and obese, previously sedentary women with PCOS were recruited from the community and randomised to complete either 12 weeks of moderate intensity continuous cycling exercise (MOD; 50-60% of maximal heart rate [HR_{max}]; $n=11$) or HIIT (90-95% HR_{max} ; $n=13$). All exercise was supervised by an exercise physiologist and completed 3 times per week on a cycle ergometer. Baseline and post testing measures consisted of peak oxygen consumption (VO_{2peak}) determined by a graded maximal exercise test, insulin sensitivity determined by hyperinsulinaemic-euglycaemic clamp, body composition outcomes and anti-mullerian hormone (AMH). Enjoyment was also measured throughout the intervention using feeling scales. Significant improvements were seen for VO_{2peak} after HIIT with an average increase of $5.6 \pm 2.5 \text{ mL.kg}^{-1}.\text{min}^{-1}$ ($P=0.013$) and non-significant increases in the MOD group ($3.4 \pm 2.1 \text{ mL.kg}^{-1}.\text{min}^{-1}$; $P=0.20$). Body composition, fasting insulin and AMH values remained unchanged in both groups. Non-significant improvements in glucose infusion rate ($3.3 \pm 2.8 \text{ mg.lbmkg}^{-1}.\text{min}^{-1}$; $P=0.06$) and insulin sensitivity index (M-to-I ratio; $3.0 \pm 3.8 \text{ mg.lbmkg}^{-1}.\text{min}^{-1}[\text{mU/I}]^{-1} \times 100$; $P=0.17$) were found as a result of HIIT compared to no changes after moderate intensity exercise. Importantly, HIIT was also found to be more enjoyable than moderate intensity continuous exercise. The present study is the first to compare current exercise recommendations of moderate and vigorous intensities in women with PCOS. The results of this study provide preliminary validation of HIIT and should be considered for improving cardio-metabolic health in women with PCOS.

Adipose Tissue, Appetite, and Obesity OBESITY TREATMENT: GUT HORMONES, DRUG THERAPY, BARIATRIC SURGERY AND DIET

Studying Mechanisms of Satiety in the Human Ileum and Colon

Anya Ramgulum, PhD¹, Martina Tashkova, MBBS¹,
Maeve O'Driscoll, MRes¹, Georgia Franco Becker, PhD¹,
Hannah Stephens, MSc¹, Jesus Miguens Blanco, PhD¹,
Elaine Holmes, PhD¹, Julian R. Marchesi, PhD¹,
Dominic Blunt, MBBS², Isabel Garcia Perez, PhD¹, Gary Frost,
PhD¹, Kevin Graeme Murphy, PhD¹.

¹IMPERIAL COLLEGE LONDON, London, United Kingdom,

²Imperial College Healthcare NHS Trust, London, United Kingdom.

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Background The gut-brain axis plays important roles in the regulation of appetite and glucose homeostasis. The presence of nutrients and their digestive products in specific regions of the gastrointestinal tract modulates neuronal and hormonal signalling, including the release of the appetite-suppressing gut hormones glucagon-like peptide-1 (GLP-1) and peptide YY (PYY). While there has been significant research into the upper gut mechanisms behind satiation, i.e. the termination of meal, the role of the ileum and colon in satiety, i.e. the process which delays a subsequent meal, has been relatively little investigated, particularly in humans. **Methods** Ten healthy volunteers attended our Clinical Research Facility for two visits of four days each. At each visit they had either a nasoileal or a nasocolonic

tube inserted under fluoroscopy. They were then provided a diet rich in protein and fibre to promote satiety. Gut contents and blood samples were taken before and during test meals at the start and end of the visit, and visual analogue scales were used to measure subjective feelings of appetite. Metabonomic analysis of gut fluid was carried out using a combination of in-house NMR and LC-MS-based methods. 16S rRNA gene sequencing was used to investigate effects on the colonic microbiome. Circulating levels of glucose, the gut hormones GLP-1 and PYY, and the pancreatic hormones insulin and glucagon were measured. **Results and discussion** The test meals resulted in sustained suppression of appetite and release of GLP-1 and PYY. Ileal and colonic microbial profiles were distinct from those identified in stool samples, and changed with adaptation to the high protein and fibre diet. Integrating hormonal, metabonomic and bacterial datasets from these human studies gives insight into how nutrient and metabolite sensing in the gastrointestinal tract regulates appetite and glucose homeostasis, and may suggest novel therapeutic targets for metabolic disease.

Diabetes Mellitus and Glucose Metabolism

DIABETES COMPLICATIONS II

Worsening Diabetes Control in Breast Cancer Patients Treated with Alpelisib

Robert Geier, MD¹, Nisreen Abu Al Hommos, MD²,
Ebenezer A. Nyenwe, MD³, Anita Eapen, MD¹.

¹UTHSC, Memphis, TN, USA, ²UTHSC, Bartlett, TN, USA, ³Univ of Tennessee, Germantown, TN, USA.

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Title: Worsening Diabetes Control in Breast Cancer Patients Treated with Alpelisib

Introduction: A new phosphatidylinositol-3-kinase (PI3K) inhibitor, alpelisib (Piqray) has been recently approved for the treatment of breast cancer. Severe hyperglycemia has been reported as an adverse effect. Many breast cancer patients also have diabetes mellitus type 2 which puts them at a higher risk for this adverse effect. 1 2

Case description: Patient is a 73 year old Caucasian woman with history of insulin treated type 2 diabetes mellitus and breast cancer who presented to the hospital with a left hip fracture. She has been recently started on alpelisib with worsening glycemic control. Glycemic control improved after alpelisib was held for 5 days. She resumed taking alpelisib and had an up titration of the insulin regimen. During her hospital stay, she suffered from hyperglycemia as high as 558 mg/dl. HbA1c increased to 11.3% from 6.5% reportedly before starting alpelisib. Patient was discharged on an intensified regimen with close follow up.

Discussion: Alpelisib is a PI3K inhibitor used in the treatment of postmenopausal women and men with hormone receptor positive, human epidermal growth factor receptor-2 negative, PIK3CA-mutated metastatic breast cancer. It inhibits PI3K which in turn inhibits protein kinase B (AKT). Insulin binds to insulin receptor substrates which activates PI3K, which in turn activates AKT resulting in translocation of the glucose transporter GLUT4 to the plasma membrane causing an uptake of glucose.3