[1]Neuroendocrine Unit, Department of Medicine, Massachusetts General Hospital, Boston, MA, USA, [2]Eating Disorders Clinical and Research Program, Massachusetts General Hospital, Boston, MA, USA, [3]Department of Psychiatry, Faculty of Medicine, University of Geneva, Geneva, Switzerland, [4]Division of Women's Health, Department of Medicine and Department of Psychiatry, Brigham and Women's Hospital, Boston, MA, USA.

Objective: Avoidant/restrictive food intake disorder (ARFID) occurs across the weight spectrum, however research addressing the coexistence of ARFID with overweight/obesity (OV/OB) is lacking. We aimed to establish co-occurrence of OV/OB and ARFID and to characterize divergent neurobiological features of ARFID by weight.
Method: Youth with full/subthreshold ARFID (11 with healthy weight [HW], 12 with OV/OB) underwent fasting brain fMRI scan while viewing food/non-food images (M age = 16.92 years, 65% female, 87% white). We compared groups on BOLD response to high-calorie foods (HCF) (vs. objects) in food cue processing regions of interest. Following fMRI scanning, we evaluated subjective hunger pre- vs. post-meal. We used a mediation model to explore the association between BMI, brain activation and hunger.
Results: Participants with ARFID and OV/OB demonstrated significant hyperactivation in response to HCF (vs. objects) in the orbitofrontal cortex (OFC) and anterior insula compared with HW subjects with ARFID. Mediation analysis yielded a significant indirect effect of group (HW vs. OV/OB) on hunger via OFC activation (effect=18.39, SE=11.27, 95% CI [-45.09, -3.00]), suggesting that OFC activation mediates differences in hunger between ARFID participants with HW and OV/OB.
Conclusions: Compared to youth with ARFID and HW, those with OV/OB demonstrate hyperactivation of brain areas critical for reward value of food cues. Postprandial changes in subjective hunger depend on BMI and are mediated by OFC activation to food cues. Whether these neurobiological differences contribute to selective hyperphagia in ARFID presenting with OV/OB and represent potential treatment targets is an important area for future investigation.

Adipose Tissue, Appetite, and Obesity
INTEGRATED PHYSIOLOGY OF OBESITY AND METABOLIC DISEASE

No Differences in Metabolic Parameters Between Roux-en-Y Gastric Bypass and Sleeve Gastrectomy, Regardless of Achieved Weight Loss

Narriane Chaves Pereira Holanda, Msc[1], Mariana Braga Lacerda, MD[1], Caio Chaves de Holanda Limeira, Mr, Student[2], Heloisa Calegari Borges, Ms, Student[2], Marilia Moreira Sales, Student[1], Gabrielly de Oliveira Viana, Student[1], Arthur Gomes Cavalcante, Student[1], Igor Rosembergh Nobrega Medeiros, Student[1], Nara Nóbrega Crispim Carvalho, Msc[3], Francisco Farias Bandeira, FACE,MD[4].
[1]Universidade Federal da Paraíba, João Pessoa, Brazil, [2]UNIVERSIDADE POTIGUAR, Natal, Brazil, [3]Universidade Federal da Paraíba, JOAO PESSOA, Brazil, [4]University of Pernambuco Medical School, Recife PE, Brazil.

Background: Roux-en-y (RYGB) is considered a procedure with more malabsorptive impact than sleeve Gastrectomy (SG), so the risk of chronic complications seems greater. **Aim:** To describe the metabolic profile and weight regain of patients who underwent bariatric surgery, according to each procedure. **Method:** A retrospective cohort with patients who underwent bariatric surgery (2003–2018). The sample was divided into SG group and RYGB group. Comparisons were made to analyze the relationship between the procedure itself and metabolic improvements, weight loss and weight regain. **Results:** We included 117 eligible participants (91.5 % female, 51.2% RYGB surgery), mean follow-up was 4.4± 3.3 years. Mean age was 41.8±6.8 years, without significant difference between the groups. Before the surgery, the groups were similar according metabolic profile (fasting glucose, Hba1c, total cholesterol, LDLc, triglycerides and HOMA IR), except by non-HDLc (RYGB 108.8±26.3 vs SG 127.2±33.2 mg/dl, p=0,002) and 25OHD (RYGB 28.9±4,7 vs SG 34.3±9,5 ng/ml, p=0.044). The RYGB group had greater weight than the SG group (mean 114.1±13.5 kg vs 122.7±20.5 Kg, p<0.0001) and almost 23.3% of the participants had T2DM and 36.2% of them had systemic arterial hypertension, without significant difference between the groups. The RYGB group had a greater postoperative time than the SG group (mean 5.0±4.0 vs 3.6± 2.9 years, respectively). After the surgery, although weight loss was greater in the RYGB group than the SG group (mean 39%±10.2 *vs* 34.1%±9.8, p<0.0001, respectively), both groups were similar regarding BMI, body fat percentage (BFP) and abdominal circumference. Also, there were no differences in the metabolic profile (fasting glucose, Hba1c, HOMA IR, leptin, triglycerides and HDLc), according to the type of surgery, except in the total cholesterol and LDLc levels (RYGB 167.9±28.2 vs SG 187.9±35.1 and RYGB 92.6±25.6 vs SG 109.5±30.8). Nearly the whole sample (95%) has reached > 20% weight loss. Despite that, 37.6% of the patients have regained > 20% of weight loss, with no relation regarding the type of surgery. Only 7% of the patients remained with some degree of glucose intolerance, with no difference between the groups. **Conclusion:** We found similar benefits among metabolic markers and weight regain after SG, compared to RYGB.

Adipose Tissue, Appetite, and Obesity
INTEGRATED PHYSIOLOGY OF OBESITY AND METABOLIC DISEASE

Obesity, Body Fat Distribution, and Circulating Glutamate Concentrations, A BI-Directional Mendelian Randomization Study

Ina Maltais-Payette, PhD student, Jérôme Bourgault, Undergrad student, Benoît Arsenault, PhD, Andre Tchernof, PhD
CRIUCPQ, Québec, QC, Canada.

Background: Various observational studies have reported that circulating levels of the amino acid glutamate was significantly associated with central fat accumulation in men and women. This is the case in the Framingham Heart Study Generation 3 for waist circumference, in the TwinsUK cohort for trunk fat and in a cohort of 1449 Japanese for visceral adipose tissue area measured by computed tomography. However, whether the association between

abdominal adiposity and circulating glutamate is causal, as well as the direction of this association, is unknown. Here, we aimed to determine whether obesity and abdominal obesity were causally associated with circulating glutamate levels. **Methods:** We used a two-sample bi-directional inverse-variance weighted Mendelian randomization study design (IVW-MR). We derived summary statistics for our exposures and outcomes from published genome-wide association studies from the GIANT consortium (n = 681 275) and blood metabolites (n = 7 804). We identified independent genetic variants ($r^2 < 0.1$) associated with body mass index (BMI) and waist-to-hip ratio adjusted for BMI (WHRadjBMI, $p < 5x10^{-8}$) as well as circulating glutamate ($p < 5x10^{-5}$). **Results:** We found no causal association between circulating glutamate levels and BMI (beta = 0.082, SE = 0.0413, p = 0.0471) or WHRadjBMI (beta = -0.00106, SE = 0.0401, p = 0.979). However, there was a positive effect of BMI (beta = 0.0608, SE = 0.0150, $p = 5.19x10^{-5}$) and WHRadjBMI (beta = 0.0701, SE = 0.0198, $p = 3.98x10^{-4}$) on circulating glutamate level. **Conclusion:** This Mendelian randomization analysis suggests that obesity and abdominal obesity are causally related to elevated circulating glutamate levels. Glutamate levels are not causally related to adiposity. Whether the downregulation of branched-chain amino acid catabolism in adipose tissue reported in obesity underlies this association should be explored.

Adipose Tissue, Appetite, and Obesity
INTEGRATED PHYSIOLOGY OF OBESITY AND METABOLIC DISEASE

Once-weekly Subcutaneous Semaglutide 2.4 mg Reduces Body Weight in Adults with Overweight or Obesity Regardless of Baseline Characteristics (STEP 1)

Robert F. Kushner, MD[1], W Timothy Garvey, MD[2], Dan Hesse, PhD[3], Anna Koroleva, MD[3], Soo Lim, MD[4], Ildiko Lingvay, MD, MPH, MSCS[5], Ofri Mosenzon, MD[6], Signe OR Wallenstein, MSc[3], Thomas A. Wadden, PhD[7], Carel W. le Roux, PhD[8].

[1]Division of Endocrinology, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA, [2]Department of Nutrition Sciences, University of Alabama at Birmingham, Birmingham, AL, USA, [3]Novo Nordisk A/S, Søborg, Denmark, [4]Department of Internal Medicine, Seoul National University College of Medicine, Seoul National University Bundang Hospital, Seongnam, Korea, Republic of, [5]UT Southwestern Medical Center, Dallas, TX, USA, [6]Diabetes Unit, Department of Endocrinology and Metabolism, Hadassah Medical Center, Faculty of Medicine, Hebrew University of Jerusalem, Ein Kerem, Israel, [7]Department of Psychiatry, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA, [8]Diabetes Complications Research Centre, Conway Institute, University College Dublin, Dublin, Ireland.

Background: Semaglutide is a long-acting, subcutaneous (s.c.), glucagon-like peptide-1 analogue that is currently being investigated for obesity management in adults with overweight or obesity in the phase 3 STEP clinical trial program. Varying degrees of weight loss were observed with once-weekly s.c. semaglutide 2.4 mg in STEP 1, and a post-hoc analysis was conducted to investigate weight loss in subgroups of participants based on their baseline characteristics.

Methods: STEP 1 was a randomized, double-blind, placebo-controlled, phase 3 trial (NCT03548935). Adults aged ≥18 years with either body mass index (BMI) ≥27 kg/m^2 with ≥1 weight-related comorbidity or BMI ≥30 kg/m^2, without type 2 diabetes, were randomized 2:1 to 68 weeks' treatment with once-weekly s.c. semaglutide 2.4 mg or placebo, as adjunct to lifestyle intervention. A descriptive evaluation of categorical weight loss with semaglutide from baseline to week 68 (≥20%, 15-<20%, 10-<15%, 5-<10%) by baseline characteristics (age, sex, race [White, Asian, Black or African American, other], body weight, BMI, waist circumference, and glycemic status [normo-glycemia, prediabetes]) was conducted. Mean percent weight loss with semaglutide from baseline to week 68 was analyzed separately by sex (male, female) and baseline body weight (≥115 kg, 100-<115 kg, 90-<100 kg, <90 kg) using a mixed model for repeated measurements analysis with treatment, subgroup (of sex or baseline body weight), and the interaction between treatment and subgroup as factors, and baseline body weight as a covariate, all nested within visit (based on the trial product estimand [treatment effect assuming treatment adherence and without use of rescue intervention] for the on-treatment period).

Results: STEP 1 included 1,961 randomized participants (mean age 46 years, body weight 105.3 kg, BMI 37.9 kg/m^2; 74.1% female). For categorical weight loss, the observed proportions of participants with ≥20%, 15-<20%, 10-<15%, and 5-<10% weight loss at week 68 were 34.8%, 19.9%, 20.0%, and 17.5% with semaglutide vs 2.0%, 3.0%, 6.8%, and 21.2% with placebo, respectively. The distribution of participants across weight loss groups did not appear to be affected by any baseline characteristics, except sex and baseline body weight. Mean percent weight loss at week 68 with semaglutide was greater among females than males, and in participants with lower vs higher baseline body weight. Sex and baseline body weight were independently associated with weight loss with semaglutide vs placebo at week 68 ($p<0.001$ for both tests for subgroup interactions).

Conclusion: In STEP 1, weight loss with once-weekly s.c. semaglutide 2.4 mg was seen in all subgroups evaluated, and was generally not influenced by baseline characteristics. The exception was sex and baseline body weight; female sex and a low baseline body weight were associated with a greater response to semaglutide.

Adipose Tissue, Appetite, and Obesity
INTEGRATED PHYSIOLOGY OF OBESITY AND METABOLIC DISEASE

Prevalence of Childhood Obesity in the United States 1999 - 2018: A 20-Year Analysis

Hang Long Li, BSc[1], Man Fung Tsoi, PhD[1], Qi Feng, PhD[2], Ching-Lung Cheung, BSC,PhD[3], Tommy Cheung, FRCP[1], Bernard MY Cheung, PhD[1].

[1]Department of Medicine, The University of Hong Kong, Hong Kong, Hong Kong, [2]Jockey Club School of Public Health and Primary Care, The Chinese University of Hong Kong, Hong Kong, Hong Kong, [3]The University of Hong Kong, Hong Kong, Hong Kong.