

procedure by bioimpedance using the SECA mBCA525 body analyzer. At the same time, biochemical metabolic markers were determined (fasting glucose, HOMA, HbA1c, CT, HDL, LDL, and triglycerides). The results were reported using descriptive statistics. A Pearson or Spearman correlation was carried out according to the distribution of the variables.  $P < 0.05$  was taken as significant. **Results:** Eleven patients with a mean age of  $49 \pm 7$  years were included, 73% of them were women. Their average initial BMI was  $42 \pm 4$  kg/m<sup>2</sup>. VAT prior to surgery had a mean of  $10.6 \pm 2.5$  L for men and  $6.4 \pm 2.4$  L for women. Eighty-two percent of the patients fulfilled harmonized criteria for metabolic syndrome. There was a statistically significant decrease in VAT at 3 and 6 months after surgery in both men and women (Baseline  $7.5 \pm 3$  L, 3 months  $3.8 \pm 2.8$  L ( $p < 0.001$ ), 6 months  $2.5 \pm 2$  L ( $p = 0.001$ ). An average decrease in visceral adipose tissue of  $57 \pm 24\%$  in women and  $34 \pm 18\%$  in men ( $p = 0.18$ ) was found 3 months after surgery and  $70 \pm 22\%$  in women and  $60 \pm 21\%$  in men ( $p = 0.53$ ) 6 months after surgery. Laparoscopic one-anastomosis gastric bypass (OAGB) was the type of surgery with the highest percentage of VAT loss at 3 and 6 months, however, this was not statistically significant when compared with Y-Roux Gastric bypass (YRGB). A statistically significant decrease in HbA1c, HOMA, total cholesterol, LDL, and triglycerides levels were found at 3 and 6 months after surgery. However, when correlating the proportion of VAT lost with the metabolic variables, only a significant correlation was found with the HbA1c levels. The higher the proportion of VAT lost, the lower the HbA1c levels ( $R^2 -0.72$   $p = 0.01$ ). **Conclusions:** Bariatric surgery produces a statistically significant reduction in visceral adipose tissue from 3 months after surgery. In this study, an inversely proportional correlation was found between the proportion of VAT lost and HbA1c levels.

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

### *Clinically-Relevant Weight Loss is Achieved Independently of Early Weight Loss Response to Once- Weekly Subcutaneous Semaglutide 2.4 MG (STEP 4)*

Ofri Mosenzon, MD<sup>1</sup>, W Timothy Garvey, MD<sup>2</sup>, Dan Hesse, PhD<sup>3</sup>, Anna Koroleva, MD<sup>3</sup>, Robert F. Kushner, MD<sup>4</sup>, Soo Lim, MD<sup>5</sup>, Ildiko Lingvaj, MD, MPH, MSCS<sup>6</sup>, Signe OR Wallenstein, MSc<sup>3</sup>, Thomas A. Wadden, PhD<sup>7</sup>, Carel W. Le Roux, PhD<sup>8</sup>

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

**Background:** Semaglutide, a glucagon-like peptide-1 analogue, is being investigated in people with overweight

or obesity. A post-hoc analysis of the STEP 4 trial was conducted to identify whether early weight loss is predictive of later weight loss with maintenance once-weekly subcutaneous (s.c.) semaglutide 2.4 mg.

**Methods:** STEP 4 was a randomized, double-blind, phase 3 withdrawal trial (NCT03548987). Adults aged  $\geq 18$  years with either body mass index (BMI)  $\geq 27$  kg/m<sup>2</sup> with  $\geq 1$  weight-related comorbidity or BMI  $\geq 30$  kg/m<sup>2</sup>, without type 2 diabetes, underwent a 20-week run-in period. Participants reaching the maintenance dose of once-weekly s.c. semaglutide 2.4 mg at week 20 (regardless of weight loss achieved) were randomized 2:1 to semaglutide 2.4 mg or placebo, as adjunct to lifestyle intervention, for an additional 48 weeks. Percent change in body weight from week 0 to 68 was estimated using a mixed model for repeated measurements analysis with treatment, week 20 responder status, and the interaction between treatment and week 20 responder status 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). Participants were considered responders if they achieved  $\geq 5\%$  weight loss at week 20. Whether the week 20 response to semaglutide predicted the achievement of clinically-relevant weight loss ( $\geq 5\%$ ) by week 68 was also assessed.

**Results:** In STEP 4, 902 participants initiated semaglutide at week 0, of whom 803 were randomized at week 20 (semaglutide:  $n=535$ , placebo:  $n=268$ ; characteristics at week 0 for all randomized participants: mean age 46 years, body weight 107.2 kg, BMI 38.4 kg/m<sup>2</sup>; 79.0% female; 83.7% white). For the 88.0% of participants randomized to semaglutide and who were responders at week 20, mean body weight change from week 0 to 68 was -19.7%. For non-responders at week 20, mean body weight change was -6.4% with continued semaglutide vs -0.3% with switch to placebo. Of all participants randomized to semaglutide, 86.2% achieved a clinically-relevant weight loss ( $\geq 5\%$ ) at week 68. Being a responder at week 20 was highly predictive of achieving this outcome (positive predictive value: 96.4%), whereas being a non-responder at week 20 had limited predictive value (negative predictive value: 42.9%).

**Conclusion:** In the STEP 4 trial, the vast majority of participants who were randomized to the maintenance dose of once-weekly s.c. semaglutide 2.4 mg at week 20 had lost  $\geq 5\%$  body weight by week 68, with most achieving this by week 20. Overall weight loss with semaglutide was greater among early responders, but non-responders also achieved a clinically-relevant weight loss by week 68 if semaglutide treatment was continued.

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

### *Developmental Changes in Food Perception and Preference*

Monica Serrano-Gonzalez, MD<sup>1</sup>, Seung-Lark Lim, PhD<sup>2</sup>, Nicolette Sullivan, PhD<sup>3</sup>, Robert Kim, BS<sup>4</sup>, Megan M. Herting, PhD<sup>5</sup>, Juan Espinoza, MD<sup>6</sup>, Christina Koppin, BA<sup>4</sup>, Joyce R. Javier, MD, MPH, MS<sup>6</sup>, Shan Luo, PhD<sup>5</sup>, Mimi S. Kim, MD MSC<sup>6</sup>.

<sup>1</sup>Warren Alpert Medical School of Brown University/Hasbro Children's Hospital, Providence, RI, USA, <sup>2</sup>University of

Missouri-Kansas City, Kansas City, MO, USA, <sup>3</sup>London School of Economics, London, United Kingdom, <sup>4</sup>Children's Hospital Los Angeles, Los Angeles, CA, USA, <sup>5</sup>Keck School of Medicine of USC, Los Angeles, CA, USA, <sup>6</sup>Keck School of Medicine of USC/Children's Hospital Los Angeles, Los Angeles, CA, USA.

Food choices are a key determinant of dietary intake, with involved brain regions such as the mesolimbic and prefrontal cortex maturing at a differential rate from childhood to young adulthood. However, developmental changes in healthy and unhealthy food perception and preference remain poorly understood. We aimed to understand this gap by investigating whether perceptions and preferences for food vary as a function of age, and how specific food attributes (i.e., taste and health) impact these age-related changes. We hypothesized that there would be an inverted U-shaped relationship between age and preference for high-calorie foods. As well, we expected that both dietary self-control and the decision weight of the health attribute would increase with age. One hundred thirty-nine participants aged 8–23 years (79 males, 60 females) participated in this study. They completed computerized rating tasks to assess taste, health, and liking (or preference) of high-calorie and low-calorie foods, followed by 100 binary food choices based on each participant's individual ratings for taste and health. Among the 100 pairs, 75 were deemed challenge trials, where one food had a higher taste rating but a lower health rating than the other food item. Dietary self-control was considered successful when the healthier food cue in the challenge trial was chosen, and self-control success ratio (SCSR) was computed as the proportion of self-control success trials over the total number of choices. Results showed that high-calorie foods were rated as more tasty ( $r = 0.32$ ,  $p < 0.001$ ) and less healthy ( $r = -0.22$ ,  $p < 0.01$ ) with increasing age. As well, older participants wanted to eat high-calorie foods more than the younger participants ( $r = 0.29$ ,  $p = 0.001$ ). Furthermore, older age was associated with an increased decision weight of taste attribute on food preferences ( $r = 0.26$ ,  $p = 0.002$ ), suggesting that the taste attribute may contribute to the age-related increases in preference for high-calorie foods. Although participants rated low-calorie foods as less tasty ( $r = -0.17$ ,  $p = 0.04$ ) and less healthy ( $r = -0.31$ ,  $p < 0.001$ ) with increasing age, there was no significant association between age and preference for low-calorie foods. Participants made faster food choices with increasing age ( $r = -0.31$ ,  $p < 0.001$ ), which was driven by failed self-control choices ( $r = -0.23$ ,  $p = 0.006$ ). There was no significant association between age and SCSR ( $p = 0.5$ ). Our results are consistent with other studies that demonstrate age-related increases in consumption of calorie-dense foods in youth, and suggest that age may be more relevant to preference for high-calorie than low-calorie foods. Future studies are merited to investigate the neurobiology underlying these developmental changes in food perceptions and preferences.

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

*Diabetes and Insulin Resistance Show Association With Femoral Instead of Abdominal Adipocyte Size in Asian Indians*

Rahul Sahlot, DM, Anshul Kumar, DM, Pradeep Tiwari, PHD, Nitish Mathur, MD, Himanshu Sharma, DM endocrinology, Naincy Purwar, DM, Sandeep Kumar Mathur, MD, DM SMS MEDICAL COLLEGE, Jaipur, India.

**Objectives:** Energy intake exceeding expenditure results in adipogenesis, which consists of adipocyte hyperplasia and hypertrophy. Adipocyte hypertrophy is the pathological hallmark of 'sick fat' responsible for the development of insulin resistance and diabetes mellitus. In Asian Indians, who show a thin, fat phenotype, the association of adipocyte hypertrophy in various fat depots with insulin resistance and diabetes is not precisely known. The objective of this study is to find an association between adipocyte size of abdominal and thigh fat depot and certain parameters of diabetes mellitus. **Material & Methods:** In this cross-sectional analytical study, 172 patients were recruited. Abdominal subcutaneous and visceral fat samples were available of 100 patients (Non-diabetics: 56; Diabetics: 44), whereas thigh fat was analyzed in 72 patients (Non-diabetics: 40; Diabetics: 32). All participants had a BMI of less than 30 kg/m<sup>2</sup> to negate the effect of obesity on adipocyte size. Fasting glucose, insulin, HbA1c, lipid profile including triglycerides, and total cholesterol were measured in all participants, and HOMA-IR was calculated. Adipocyte size in biopsied tissue after fixation was measured with the help of Motic Panthera Moticam 5 trinocular microscope (BA210LED) and Adobe Photoshop CC image analysis tool. **Results:** Mean adipocyte size in abdominal visceral compartment in diabetics and non-diabetics were  $16610.3 \pm 889.5 \text{ um}^2$  and  $16129.8 \pm 878.5 \text{ um}^2$  respectively. Whereas, mean adipocyte size in abdominal subcutaneous fat in diabetics and non-diabetics were  $15071.0 \pm 1261.1 \text{ um}^2$  and  $14356.8 \pm 1004.7 \text{ um}^2$  respectively. Adipocyte size difference of both the abdominal compartments between diabetic and non-diabetic group was statistically non-significant ( $p = 0.70$  &  $0.65$  in omental and abdominal subcutaneous compartments respectively). Mean adipocyte size of thigh in diabetics and non-diabetics were  $13070.2 \pm 1416.2 \text{ um}^2$  and  $9020.1 \pm 811.1 \text{ um}^2$  respectively and difference between adipocyte size between both groups was statistically significant ( $p = 0.01$ ). Thigh Adipocyte size in diabetic subgroup was positively correlated with HOMA-IR ( $r = 0.4$ ,  $p = 0.02$ ), triglycerides ( $r = 0.4$ ,  $p = 0.03$ ), waist circumference ( $r = 0.32$ ,  $p = 0.03$ ). On multivariate linear regression analysis HOMA-IR ( $\beta = 0.45$ ,  $p = 0.00$ ), triglycerides ( $\beta = 0.38$ ,  $p = 0.01$ ) and waist circumference ( $\beta = 0.35$ ,  $p = 0.02$ ) are predictor of increased adipocyte size. **Conclusion:** We found that thigh adipocyte size was significantly larger in diabetics in comparison to non-diabetics, whereas no such difference was found in the abdominal fat compartment. In diabetic patients' thigh, adipocyte size was positively correlated with HOMA-IR, waist circumference, and triglyceride levels, underlining the role of peripheral fat depots in the pathogenesis of diabetes type 2.

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

*Effect of Time-Restricted Feeding on Body Weight and Cardiometabolic Risks: A Systematic Review and Meta-Analysis of Randomized Controlled Trials*