p = 0.002; and in WHR: 0.97 ± 0.07 vs 1.01 ± 0.07, p = 0.027. **Conclusion:** We found that increased levels of SCL were associated with WHR and TG in T2DM patients with DPN.

Diabetes Mellitus and Glucose Metabolism

BENCH TO BEDSIDE: NOVEL MECHANISMS IN DIABETES AND METABOLISM

Sex Disparities in Thermoregulatory and Metabolic Responses to Mild Cold Exposure Largely Explained by Differences in Body Mass and Body Surface Area

Yoanna M. Ivanova, MSc[1], Tracy Swibas, MS[2], François Haman, PhD[3], Kerry L. Hildreth, MD[2], Yubin Miao, PhD[4], Wendy M. Kohrt, PhD[4], Andre Carpentier, MD, FRCP[5], Edward L. Melanson, PhD[6], Denis P. Blondin, PhD[7].
[1]UNIVERSITE DE SHERBROOKE, Sherbrooke, QC, Canada, [2]University of Colorado Denver, Aurora, CO, USA, [3]University of Ottawa, Ottawa, ON, Canada, [4]University of Colorado School of Medicine, Aurora, CO, USA, [5]Center Hospital University de Sherbrooke, Sherbrooke, QC, Canada, [6]University OF CO Health Science Center, Aurora, CO, USA, [7]Universit de Sherbrooke, Sherbrooke, QC, Canada.

Sex-related differences in thermoregulatory responses to cold exposure, such as differences in metabolic heat production and fuel selection, are often attributed to differences in morphology and body composition. Whether these differences persist in response to cold when comparing lean, healthy men and women with equivalent total body mass (BM, heat producing capacity) and body surface areas (BSA, heat loss capacity) remains unknown. In this study, we aimed to compare thermoregulatory and metabolic responses to cold exposure in both men and women, before and after matching for BM (± 0.6 kg) and BSA (± 0.01 m^2). Data included in this study were derived from four previously published studies and an additional 13 men and 23 women who recently completed an identical 3h mild cold exposure protocol. Included in the analyses were 45 healthy men and 23 healthy women [27 years (95% CI: 25 to 28) in men *vs.* 34 years (95% CI: 30 to 38) in women, $P = 0.0003$], including 7 men and women of the same age [28 years (95% CI: 22 to 34) *vs.* 29 years (95% CI: 22 to 37), $P = 0.78$] matched for BM and BSA. Using a combination of indirect calorimetry, electromyography and positron emission tomography with ^{11}C-acetate and ^{18}F-fluorodeoxyglucose, we quantified mean skin temperature, whole-body energy expenditure (EE), shivering intensity, brown adipose tissue (BAT) oxidative metabolism and glucose uptake. The cold-induced decrease in mean skin temperature was greater in women than men [-6.4°C (95% CI: -6.7 to -6.0) *vs.* -5.4°C (95% CI: -5.8 to -5.1), $P = 0.0004$], whereas EE was higher in men compared to women both during room temperature and cold exposure, with the cold-induced increase in EE being slightly greater in men than women [3.8 kJ·min^{-1} (95% CI: 3.2 to 4.5) *vs.* 2.8 kJ·min^{-1} (95% CI: 2.0 to 3.7), $P = 0.07$]. In contrast, shivering intensity (%MVC) was higher in women compared to men [3.0 %MVC (95% CI: 2.1 to 3.8) *vs.*1.8 %MVC (95% CI: 1.5 to 2.2), $P = 0.0069$]. Cold exposure also increased BAT oxidative index to a similar magnitude in men and women, increasing ~4-fold in men and ~3-fold in women (effect of sex, $P = 0.2067$). Both fractional glucose uptake [0.022 min^{-1} (95%CI: 0.017 to 0.027) in men and 0.021 min^{-1} (95%CI: 0.013 to 0.030) in women, $P = 0.02$] and net glucose uptake in BAT [92 nmol.g^{-1}.min^{-1} (95%CI: 69 to 115) in men and 91 nmol.g^{-1}.min^{-1} (95%CI: 53 to 129) in women] were not different between the sexes without or with matching for BM and BSA. The sex differences in mean skin temperature, energy expenditure and shivering intensity were all lost once participants were matched for BM and BSA. The present results suggest that much of the sexual dimorphism in thermoregulatory and metabolic responses to mild cold exposure can be explained by differences in BM and BSA.

Diabetes Mellitus and Glucose Metabolism

BENCH TO BEDSIDE: NOVEL MECHANISMS IN DIABETES AND METABOLISM

The Role of Inositol Phosphate Multikinase (IPMK) in Time Restricted Feeding in Animal Model

Ik-Rak Jung, PhD, Becky Tu-Sekine, PhD, Frederick Anokye-Danso, PhD, Rexford S. Ahima, MD, PhD, Sangwon Kim, PhD.
Johns Hopkins University, Baltimore, MD, USA.

Obesity is a major public health problem of the U.S. and is associated with diabetes, cardiovascular diseases and other diseases. Most research studies focus on excessive food consumption as the main cause of obesity. However, emerging data indicate that the timing of feeding can have significant effects on body weight and metabolism. Numerous studies in animals and small clinical studies in humans have shown that eating erratically over the 24 hour period or out of phase with the circadian rhythm predisposes toward weight gain, steatosis, dyslipidemia, insulin resistance and diabetes. Furthermore, studies indicate that restricting food intake to the active period synchronizes the circadian rhythm and metabolism, enhances weight loss and improves metabolic outcomes. Time restricted feeding (TRF) increases the amplitudes of clock gene expression and pathways mediating nutrient sensing and hepatic metabolism. However, the mechanisms mediating the effects of TRF are not fully understood. Here we characterized mice (10 week-old) fed a high-fat diet ad libitum (ALF) or from 7 pm to 7 am (TRF) for 2 weeks. The basal glucose production rate was similar between the two groups. Under hyperinsulinemic-euglycemic clamp, the glucose infusion rate (GIR) was significantly greater in TRF group compared to ALF group indicating an increase in insulin sensitivity. Using radioisotopic tracers, we demonstrated that the hepatic glucose production (HGP) was significantly reduced and the glucose disappearance rate was increased in TRF group compared to ALF group. Moreover, a biochemical analyses of liver tissues revealed that Inositol phosphate multikinase (IPMK) act as a key enzyme for inositol polyphosphate biosynthesis and play a role in insulin-, nutrient-, and energy-mediated metabolic signaling, was increased during TRF. Moreover, deletion of IPMK in hepatocytes decreased insulin stimulated AKT phosphorylation while increased lipid accumulation and gluconeogenesis. Importantly, hepatic deletion of IPMK attenuated the beneficial effects of TRF suggesting that