T2:P2a-013
DIFFERENT EFFECT OF HIGH SUCROSE DIET ON LIPOGENESIS AND ANTI-LIPOLYTIC INSULIN ACTION IN LEAN AND OBSESE RATS
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Aims: Our aim was to investigate the effect of high sucrose (HS) diet on the development of insulin resistance (IR) in SHROB/Kol rats, a model of metabolic syndrome associated with obesity.

Methods: Male SHROB/lean (L) and SHROB/Kol (OB) (b/wt. 280 ± 10 and 640 ± 24 g, resp.) were fed HS diet for 1 week. At the end of this period, the effect of a single oral glucose load on serum glucose, NEFA and TG was determined. The in vitro lipolysis was assessed as glycero release, the lipogenesis as the incorporation of 14C-gluco into lipids in EAT.

Results: One week of HS feeding resulted in significant (p < 0.05) increase of AUC (expressed as the difference of AUC before and after diet, mmol dmol (0.02 nM) per mg) in OB rats. The 
AUC_t in OB rats was 1.4 ± 0.3 vs 2 ± 0.2, AUC_15 min was 29 ± 4 vs 2 ± 5, AUC_15-30 min was 4 ± ± ± vs 28 ± 5. Insulin-tolerant test showed the decreased antilipolytic effect of insulin measured as AUC:CER in OB rats (78 ± 7 vs 50 ± 9 nmol/l/120 min). Under in vitro conditions in OB compared to L rats, the adiponectin-stimulated lipolysis was decreased, insulin did not exert its antilipolytic effect and the insulin-stimulated lipogenesis was reduced.

Conclusions: The metabolic disturbances in glucose and lipid metabolism induced by increased sucrose supply were more severe in obese than lean rats. The increased serum NEFA concentrations that contribute to the establishment of IR may result from failure of insulin-stimulated suppression of adipose tissue lipolysis and insulin-stimulated lipogenesis.

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THE ANTIFUNGAL AGENT KETOCONAZOLE PROTECTS AGAINST ADIPOSY INduced BY A CAFETERIA DIET
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Aims: The purpose of this work was to study in rats the possible preventive effect of the anti-glucocorticoid agent Ketoconazole (KCCZ) against the adiposity induced by a high-fat diet (Cafeteria).

Methods: Female Wistar rats were fed on standard pelleted diet or cafeteria diet during 42 days in the presence or absence of an oral treatment with KCCZ (24 mg/kg of body weight). At the end of the experimental period, body composition was analyzed, and ex vivo lipolytic activity was assayed in the absence or presence of the beta-adrenergic agonist isoproterenol in adipocytes from perivisceral fat tissue.

Results: The cafeteria diet induced hyperphagia and an increase in the body weight gain. In addition, the total body fat and the weight of the adipose tissue deposits (perivisceral, retroperitoneal and subcutaneous) were increased by the consumption of the high-fat diet. Interestingly, KCCZ was able to prevent against the increased total body fat and the enlargement of the adipose depots induced by the cafeteria feeding. Moreover, the isoproterenol-induced ex vivo lipolysis was reduced in the adipocytes from the cafeteria-fed animals and this decrease was reverted by the treatment with KCCZ.

Conclusions: The antiguocorticoid agent KCCZ was able to protect against the adiposity induced by a cafeteria diet, revealing an interaction between fat intake and glucocorticoids on adipose deposition.

T2:P2a-015
HYPERINSULINISM IMPAIRS INSULIN-MEDIATED GLUCOSE TRANSPORT DUE TO A DISASSOCIATION OF PI3K/AKT ACTIVATION
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Aims: To assess whether hyperinsulinism, a common finding of obesity and type 2 diabetes, impairs insulin signalling, we evaluated insulin resistance in response to acute exposure to insulin (10 nM per 10 min) in human myoblasts grown (4-6 wk) in the presence of low (107 pM; SKMC-L) or high (1430 pM; SKMC-H) insulin levels and normal glucose concentration (5.5 mM).

Methods: PI3K activity was determined by immunoprecipitation with IRS-1. Protein expression and phosphorylation were determined by Western blot.

Glucose transport was measured by 2DG-H uptake.

Results: Insulin stimulation of SKMC-L was associated with increased insulin receptor (IR 77%), and IRS-1 (100%) phosphorylation, increase in PI3K (97%) and Akt (40%) activity, and caused a 73% increase in glucose transport.

After the basal incubation period, SKMC-H showed a marked upregulation of insulin receptor activity, and IRS-1 (100%) phosphorylation, increase in PI3K (97%) and Akt (40%) activity, and caused a 73% increase in glucose transport.

Conclusions: Hyperinsulinism causes desensitization of insulin-mediated glucose metabolism, associated with basal upregulation of many steps of insulin signalling, with the exception of Akt, with no further activation upon acute insulin stimulation. Our data indicate that desensitization could be the consequence of a dissociation between the activation of PI3K and Akt.

T2:P2a-016
IMPAIRED GLUCOSE TOLERANCE (IGT): SKELETAL MUSCLE FATTY ACID HANDLING AFTER A MIXED MEAL BEFORE AND AFTER WEIGHT LOSS
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Aims: Does metabolic flexibility, expressed as the capacity to switch between fuels (carbohydrate (CHO), fat) in response to a mixed meal, improve in IG men after weight loss?

Methods: Skeletal muscle substrate metabolism was studied in 8 IGT men during baseline, and after a high-fat, mixed meal. We used muscle indirect calorimetry and the forearm balance technique. Insulin sensitivity was measured with a hyperinsulinenic euglycemic clamp. The men followed an 8-week diet. Measurements were done after at least 2 weeks of energy balance. Delta’s (Δ) are baseline - total AUC/min.

Results: The men lost 14.0 ± 4.3 kg of body weight. Insulin sensitivity improved after weight loss (WL), the M-value pre-WL was 21.7 ± 10.0 and increased to 37.9 ± 11.6 mmol/min-1kgFFM-1 (p<0.01). The respiratory quotient (CO2/Oxygen consumption) in skeletal muscle during fasting was lowered after WL (pre-WL > 8.56±0.07, p=0.03). The differences in local muscle QR in response to a high-fat load (pre-WL AQR=0.03±0.05 and post-WL AR=0.05±0.16) were attributable to a trend in a higher increase in CHO oxidation (p=0.07) and a tendency for stronger suppression of fat oxidation after the high-fat meal.

Conclusions: Weight loss in subjects with impaired glucose tolerance increases insulin sensitivity and improves the capacity to switch between fuels in the skeletal muscle after a high-fat meal, as reflected by a stronger increase in CHO oxidation and a better suppression of the fat oxidation.