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Background: Serum uric acid (SUA) is related to cardiometabolic conditions such as insulin resistance (IR) and visceral adipose tissue (VAT) accumulation, which have a thoroughly explored bidirectional relationship. Here, we aimed to clarify the nature of the role uric acid plays inside this relationship, alongside the underlying causality mechanism.
Methods: We conducted a population-based cross-sectional study comprising 8,504 subjects from a joint cohort composed from both NHANES 2003–2004 and 2011–2012 cycles and ENSANUT Medio Camino 2016. We performed mixed effects linear regression models using HOMA2-IR, adipoIR, and METS-VF as indicators of both peripheral and adipose tissue IR and VAT accumulation, indicating the subject's cohort of origin as a random effect. Furthermore, we performed multiple mediation analyses to assess a potential causal mechanism and ROC curves to establish cut-off points for identification of IR and visceral obesity using SUA. Finally, with an additional dataset comprised of 226 subjects with both euglycemic hyperinsulinemic clamp (EHC) and dual X-ray absorptiometry (DXA) measurements for IR and VAT accumulation, we performed a network of confirmatory mediation analyses including adiponectin measurements. **Results:** We found that SUA has a mediating role inside the bidirectional relationship between IR and visceral obesity, and it is part of an underlying causality mechanism which includes adiponectin. The proportion of the mechanism mediated by SUA is greater when stated that IR (in either peripheral or adipose tissue) leads to VAT accumulation (14.90%[13.20%-17.00%] and 15.54%[13.61%-18.00%]) instead of the opposite direction (4.88%[3.06%-7.00%] and 8.13%[5.91%-10.00%]). This result was strengthened by a mediation analysis network using the gold-standard measurements where we observed that the joint effect of SUA and adiponectin mediated 16.32% [8.84%-26.00%] for the effect of IR and VAT accumulation and 12.52% [3.23%-23.00%] in the opposite direction. Cut-off points for SUA to predict peripheral IR were 6.1 mg/dL and 4.8 mg/dL, for males and females respectively. For visceral obesity, cut-offs were 6.4 mg/dL and 4.8 mg/dL for males and females. SUA had a high negative predictive value for all assessments.
Conclusions: Elevated SUA acts as mediator inside the bidirectional relationship between IR and VAT accumulation. Its role appears to be larger when considering adipose tissue IR as the promoter for VAT accumulation.

Adipose Tissue, Appetite, and Obesity
NOVEL MECHANISMS CONTROLLING ADIPOSE TISSUE PHYSIOLOGY AND ENERGY BALANCE
Environmental Enrichment Potentiates Glucose-Induced Anorexia in Mice

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The hypothalamus controls food intake and metabolism by integrating nutrient and hormonal signals from peripheral tissues. Both central and peripheral administration of glucose leads to a reduction in food intake in rodents. Similarly, administration of the adipocyte hormone leptin or the gastrointestinal hormone xenin reduces food intake. In contrast, impairments in hypothalamic signaling of these factors cause hyperphagia and obesity in rodents and humans. Environmental factors affect behavior including feeding behavior and energy metabolism in rodents and humans. Studies have found that environmental enrichment (EE), in which mice interact with complex sensory and motor stimulation, led to a significant reduction in adiposity and resistance to diet-induced obesity in mice. This effect is independent of energy expenditure and is associated with enhanced hypothalamic signaling, but the exact mechanism is unknown. We hypothesized that EE potentiates the feeding suppressing effects of anorectic signals. To address this hypothesis, 4-week-old male C57BL/6 mice were group housed (5/cage) under standard laboratory conditions or EE conditions with free access to regular rodent chow and feeding response to glucose, leptin and xenin was examined. EE cages were supplemented with a house, running wheels, igloos, wood logs, maze and nesting materials. Four weeks after initiating EE protocol, mice were fasted for 8 h and received an intraperitoneal injection of glucose (2 mg/g b.w.) or saline just before the onset of the dark phase. Treatment assignments were reversed for the second injection so that each animal received both treatments with a washout period of 1 week. Mice were given food immediately after the injection and food intake was measured for 4 h after the injection at 0.5–1 h intervals. The same design was repeated using leptin (2.5 μg/g b.w.) and xenin (15 or 50 μg/g b.w.). Glucose injection caused a significant reduction of food intake in both control and EE mice. However, anorexic effect of glucose was more significant in EE group compared to the control group (main effect of treatment: $P = 0.0016$ for control and $P < 0.0001$ for EE, two-way ANOVA). Significant reductions in food intake were observed between 0.5 and 2.5 h after glucose injection in EE mice, while no significant reduction was observed thereafter. Moreover, three-way ANOVA showed a significant interaction between housing condition and treatment ($P = 0.0086$). In contrast, although both leptin and xenin caused a significant reduction in food intake, there was no significant interaction between housing condition and treatment. These data suggest that environmental enrichment enhances the anorectic action of glucose without altering feeding response to leptin and xenin. It is speculated that enhanced hypothalamic glucose sensing may mediate beneficial effects of environmental enrichment on metabolism.

Adipose Tissue, Appetite, and Obesity
NOVEL MECHANISMS CONTROLLING ADIPOSE TISSUE PHYSIOLOGY AND ENERGY BALANCE
Exposure to the Widely Used Pyrethroid Pesticide Deltamethrin, Does Not Exacerbate High Fat Diet Induced Obesity or Insulin Resistance in C57BL/6J Mice

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Deltamethrin is a commonly used pesticide for the control of mosquito populations. Despite widespread use, the effects of deltamethrin on adiposity and glucose homeostasis have been equivocal with some studies showing increased, decreased and no effect on adiposity and glycemic control. However, no study to date has investigated the effect of deltamethrin in mice housed at thermoneutral temperatures, which is important for modelling metabolic diseases in rodents due to reduced thermal stress and constitutive activation of brown adipose tissue. In the current study we demonstrate for the first time that deltamethrin reduces uncoupling protein-1 expression in brown adipocytes cultured in vitro at concentrations as low as 1pm. Meanwhile, in-vivo deltamethrin does not appear to alter glycemic control or promote adiposity at exposures equivalent to 0.01, 0.1 or 1.0 mg/kg/day. Together, our study demonstrates environmentally relevant exposure to deltamethrin does not exacerbate diet induced obesity or insulin resistance.

Adipose Tissue, Appetite, and Obesity

NOVEL MECHANISMS CONTROLLING ADIPOSE TISSUE PHYSIOLOGY AND ENERGY BALANCE

Fatty Acids Modify the MicroRNA Content of Exosomes Released by Hypothalamic Astrocytes and the Response of POMC Neurons to These Exosomes

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It is now clear that hypothalamic astrocytes participate in maintaining metabolic homeostasis. Both nutrients and metabolic hormones can directly impact on these glial cells to modify their release of gliotransmitters, metabolic factors, growth factors, etc, as well as their physical interaction with neighboring neurons. Another mechanism by which astrocytes could communicate with neurons is through their release of exosomes. We have previously shown (by RNAseq analysis) that exposure to palmitic acid (PA) dramatically modifies the miRNA content of exosomes released by hypothalamic astrocytes. Here our objectives were: 1) To determine if the miRNA changes in hypothalamic astrocyte-derived exosomes in response to oleic acid (OA) differ from those seen in response to PA and 2) Analyze the response of POMC neurons to exosomes derived from astrocytes exposed to either PA or OA. Primary hypothalamic astrocyte cultures were treated with PA (0.5 mM), OA (0.5 mM) or vehicle (V) for 24 hours. Exosomes were purified from the media and used for miRNA analysis and to treat a POMC neuronal cell line (mHypoA-POMC/GFP-1). Both OA and PA modified miRNA levels in exosomes compared to those detected in V exosomes, but these modifications differed between the two fatty acids. Furthermore, the response of POMC neurons to exosomes from vehicle (E-V), OA (E-OA) and PA (E-PA) treated astrocytes for 24 hours differed significantly. The expression of POMC mRNA was significantly decreased in response to E-V and increased in response to both E-OA and E-PA, although the increase in POMC mRNA was significantly greater in E-PA treated neurons. These results suggest that hypothalamic astrocytes can directly communicate with neurons involved in metabolic control through exosomes and that the messages contained within these exosomes are modulated by the nutrient environment.

Adipose Tissue, Appetite, and Obesity

NOVEL MECHANISMS CONTROLLING ADIPOSE TISSUE PHYSIOLOGY AND ENERGY BALANCE

Feed Consumption and Weight Gain in Diabetic and Non-Diabetic Rats Treated With Azadirachta Indica (Neem) and Plathymenia Reticulata

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Introduction: Neem (*Azadirachta indica A. Juss, Meliaceae*) is a tree native to India that has several medicinal effects. It has been reported that the leaves and oil of Neem seeds present antihyperglycemic/hypoglycemic activity. *Plathymenia reticulata benth*, known as "vinhático", is a Brazilian cerrado tree that has properties of pancreatic islet hyperplasia and glycemic control in diabetic rats. Objective: To verify weight gain correlating with feed intake in rats with type 1 and non-diabetic diabetes mellitus, undertreatment with *Neem and Plathymenia* and the association between them. Methodology: Diabetes was induced by intraperitoneal streptozotocin (65mg/kg) administration after a 24-hour fast. The diagnosis was made using a blood glucose value above 200mg/dl. The study was conducted in 60 male adult Wistar rats, weighing between 180 and 220 grams, divided into 9 groups, between diabetics (DM) and non-diabetic controls (NDC), and treated with *Neem* (300 mg/kg), cold aqueous extract of *Plathymenia* (100 mg/kg), water (negative control) and insulin (3 IU/