Topic: FAT1

LONG TERM EFFECTS OF NEONATAL OVER-NUTRITION ON METABOLIC EQUILIBRIUM ARE AGE AND SEX DEPENDANT

Pilar Argente-Arizón, Purificación Ros, Francisca Díaz , Esther Fuente-Martín, David Castro-González, Vicente Barrios, Jesús Argente, Julie A. Chowen

Department of Endocrinology, Hospital Infantil Universitario Niño Jesús, Department of Paediatrics, Universidad Autónoma de Madrid, Instituto de Investigación Sanitaria La Princesa, CIBERobn, Instituto de Salud Carlos III. Madrid, Spain

The authors have nothing to declare

BACKGROUND

Neonatal over-nutrition has been demonstrated to have long-term effects on metabolism, including increased energy intake, body weight and fat mass in adulthood. However, males and females appear to be differentially affected by early over-nutrition, with little known regarding the mechanisms underlying this differential response.

It is well known that obesity in mature animals is associated with chronic systemic inflammation. However, little is known regarding the rapid responses to neonatal over-nutrition and weight gain. Indeed, how fat mass accumulation and cytokine production are affected by increased food intake may differ greatly in young animals, due at least partially to ongoing developmental processes.

HYPOTHESIS & AIM

We aimed to determine how neonatal overnutrition affects body weight (BW), body composition and cytokine levels throughout development and if these changes are sexually dimorphic. We hypothesized that the effects would be both age and sex dependant.

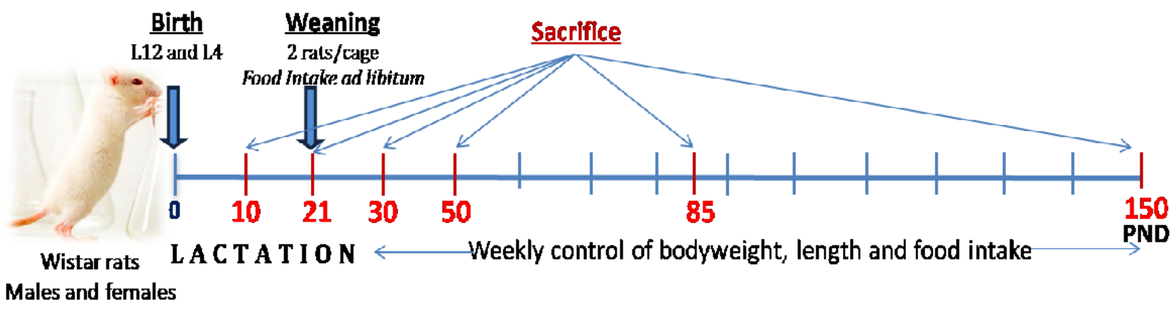
METHODOLOGY

At birth, Wistar rats were organized into litters of 4 pups/dam [(L4); over-nutrition (NON)] and 12 pups/dam [(L12); control (CT)] with equal numbers of males and females in all litters. Rats were sacrificed on postnatal days (PND) 10, 21 (weaning), 30, 50, 85 or 150.

Body weight and length were monitored on the day of birth and at sacrifice. Subcutaneous (SC) fat pads were weighed.

Serum levels of adiponectin, leptin, insulin, interleukins (IL) 6 and 1β and TNFα were measured with a multiplexed bead immunoassay.

The mRNA levels of these cytokines were quantified in SC and visceral (V) adipose tissue.



RESULTS

At PND10, BW was greater in NON rats of both sexes ($p<0.0001$; Fig.1A), continuing until PND60. After PND90, NON again increased BW in males only ($p<0.0001$). At PND10 SC was increased by NON, with females more affected than males ($p<0.0001$). These effects were not found after PND21, but at PND150 NON again increased SC in males. At PND21, NON increased V ($P<0.001$) and males had more V than females ($p<0.0001$). The effect of NON disappeared after PND50 and returned in later adulthood, but only in males. At PND10, serum glucose ($p<0.02$), insulin ($p<0.0001$), leptin ($p<0.03$) and adiponectin ($p<0.0001$) levels were increased and IL1β ($p<0.05$) and TNFα ($p<0.0006$) levels decreased by NON, with similar changes in cytokine expression in SC. None of these effects were found after PND30. Thus, there is an early effect of NON that dissipates in young adults and then reappears, but only in males, after PND90 increasing BW, V, SC, serum leptin levels and TNF-α gene expression in V.

POSTNATAL DAY 10

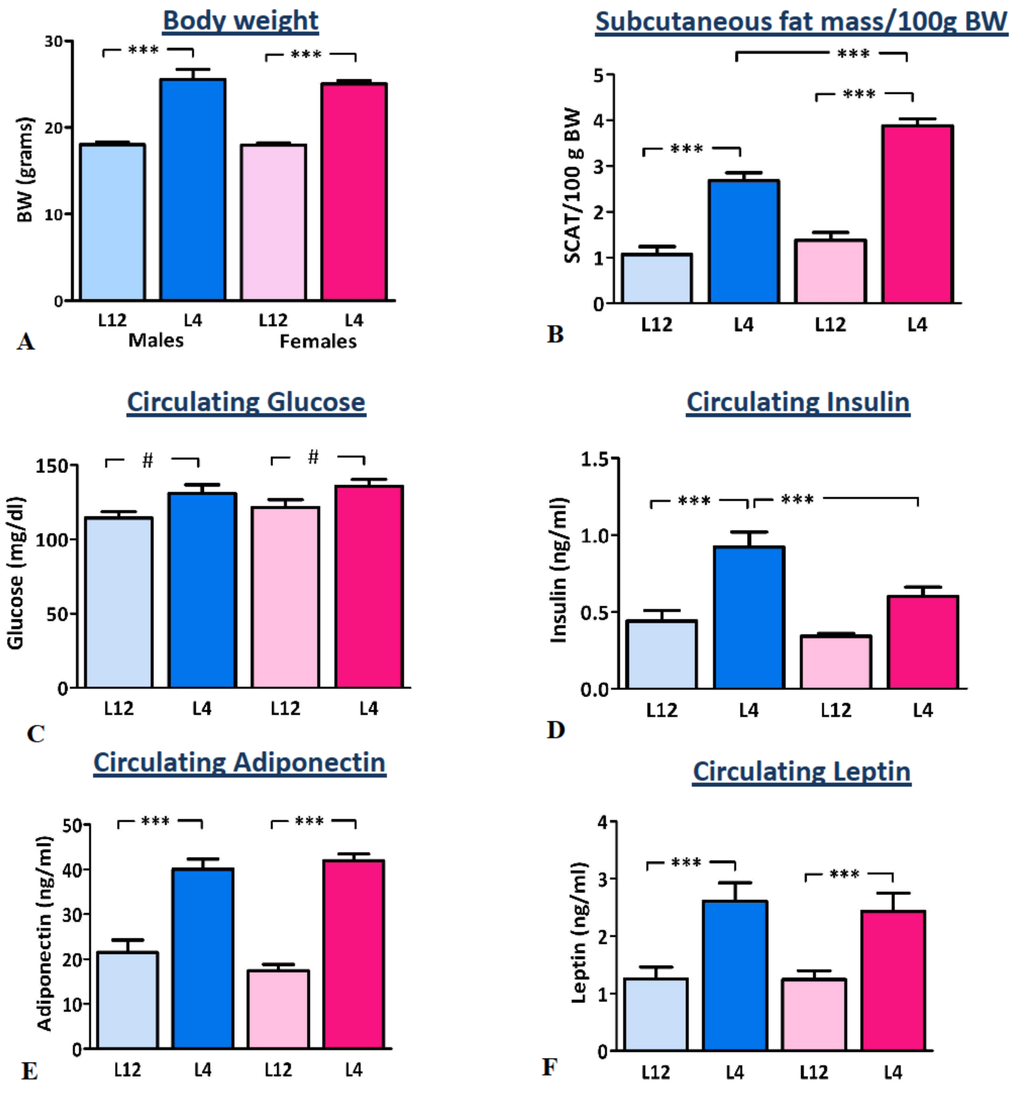


Figure 1. Body weight (A), subcutaneous adipose tissue (B), serum glucose (C), insulin (D), adiponectin (E) and leptin levels (F) of male and female rats at 10 days of age raised in litters of 12 (L12) and 4 (L4) pups/dam. ***p<0.0001, # overall litter size effect.

POSTNATAL DAY 150

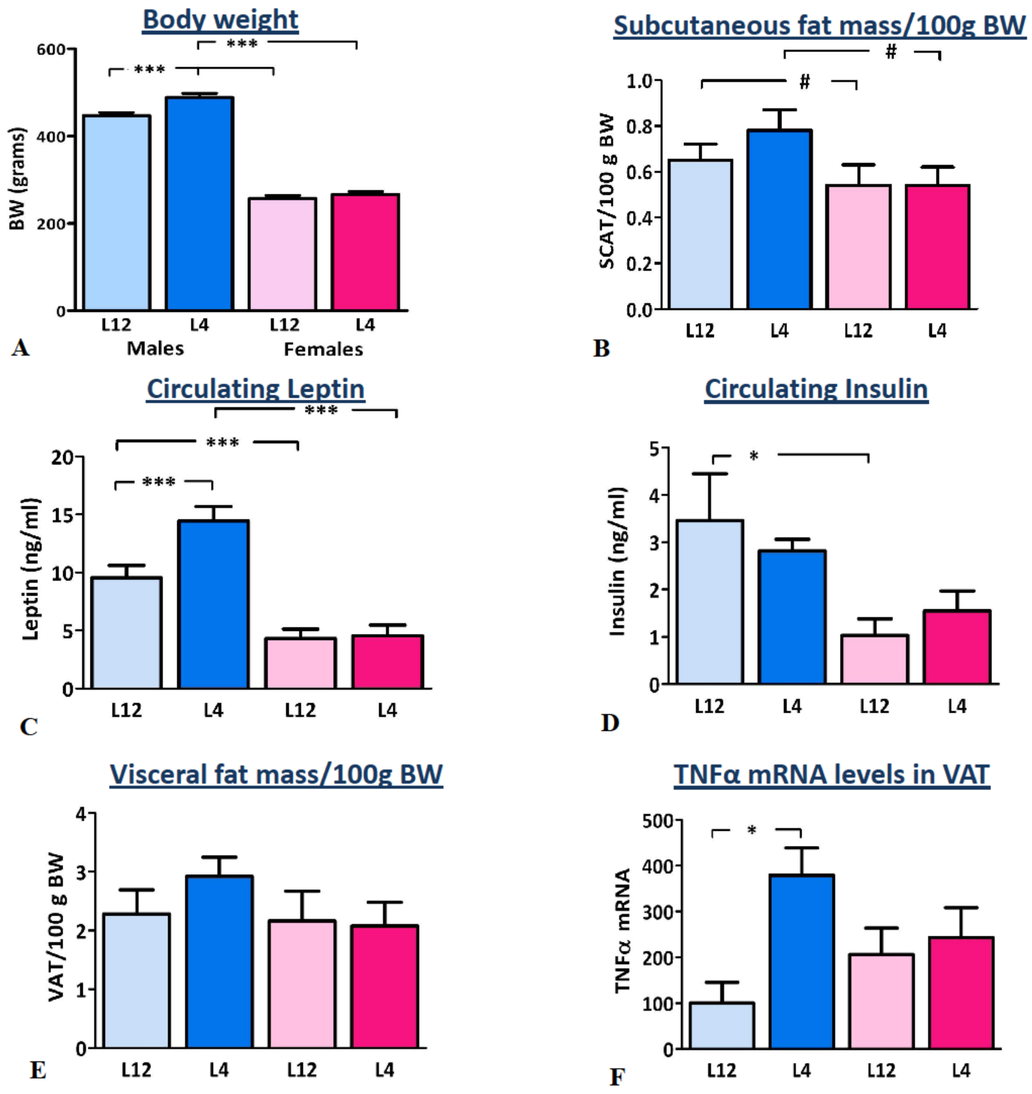


Figure 3. Body weight (A) and subcutaneous adipose tissue (B), serum leptin (C) and insulin (D) levels and amount of visceral adipose tissue (E) and TNFα mRNA levels in this adipose depot.

SUMMARY AND CONCLUSIONS: Early nutritional modifications can have long-lasting effects that are both, age and sex dependant, and that could possibly affect the aging of metabolic homeostasis. Thus, age and sex should be taken into consideration when analyzing the effects of early nutritional manipulations.

ESPE 2015 859--P3

Fat 1

Pilar Argente

DOI: 10.3252/pso.eu.54espe.2015

Poster presented at: ESPE 2015 BARCELONA European Society for Paediatric Endocrinology

PosterSessionOnline.com