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Glucose metabolism and leptin in obese women. C. Percheron^a, C. Colette^a, J. Galitzky^b, P. Barbe^b, L. Monnier^a (^aHuman Nutrition Laboratory, IURC Montpellier, 75, rue de la Cardonille, 34093 Montpellier cedex 05; ^bU 317 Toulouse, France).

Plasma leptin concentrations (PL) have been found to be associated with insulin resistance in men but not in women. We searched for an association between PL (radioimmunoassay) and insulin sensitivity (S_I , FSIVGTT, minimal model) in obese women. Twenty-seven non-diabetic obese women were included: age 39 ± 3 years, body mass index 33.2 ± 4 kg/m², fat mass (FM) 33.7 ± 6.3 kg, FM percentage 38.1 ± 3.3 (mean \pm SD). PL (35 ± 13 ng/mL) were significantly correlated with FM ($r = 0.72$, $P < 0.0001$) and FM % ($r = 0.72$) but not with S_I (10^{-4} min⁻¹ μ U⁻¹.mL, $r = 0.02$). Patients were divided into two subgroups using the S_I median (2.35). The PL concentrations were not significantly different: 36 ± 17 (group 1, $S_I = 1.3 \pm 0.6$) and 33 ± 8 (group 2, $S_I = 4.2 \pm 1.7$). In univariate analysis, PL were positively correlated to FM ($r = 0.8$, $P = 0.0003$), to FM % ($r = 0.83$, $P < 0.0001$) and to S_I ($r = 0.57$, $P = 0.04$) in group 1. In group 2, PL were positively correlated to FM ($r = 0.70$, $P = 0.006$), to FM % ($r = 0.70$), to fasting glucose ($r = 0.66$, $P = 0.03$) and negatively correlated to SI ($r = -0.57$, $P = 0.04$). In stepwise multiple regression analysis, FM % was the only predictor of PL in group 1 ($R^2 = 0.66$). In group 2, PL were positively associated with FM % (step 1), with fasting glucose (step 2), and with S_I (step 3). 79.3 % of leptin variation could be predicted by these three variables. S_I was positively associated with fasting insulinemia (step 1) and leptinemia (step 2). This preliminary data suggested a relation between leptin and glucose metabolism in obese women.

A polymorphism in the 5' untranslated region of the human *ob* gene is associated with lower leptin levels in morbid obesity. K. Clément^{a,b}, J. Hager^{a,c}, S. Francke^a, C. Dina^a, J Raison, N. Lahlou^c, A. Basdevant^b, P. Froguel^a, B. Guy-Grand^b (^aCNRS EP10/Institut Pasteur de Lille, Lille; ^bHotel-Dieu Hospital, Paris; ^cInserm U342/Saint-Vincent de Paul Hospital, Paris, France).

Many studies have shown that obesity has a considerable inherited component. Recent successes in the identification of genetic loci (particularly the *ob* gene responsible for the synthesis of leptin) in mice have resulted in a dramatic increase in information about the mechanisms controlling energy metabolism. In humans, rare cases of leptin deficiency due to a mutation in the leptin gene are associated with early onset obesity. We and others have recently reported evidence that the *ob* gene region is linked to a more common form of morbid obesity (BMI > 35 kg/m²) in humans. In this study, we screened the human *ob* gene for mutations and evaluated their putative role in obesity by a case-control association study in two independent populations of obese Caucasians. We found a DNA variant in exon 1 of the human *ob* gene (A \rightarrow G substitution, base +19). This variant was found in 62 % of our study population. Association analyses under different genetic models (dominant, co-dominant, recessive) showed no significant evidence for an association of this variant with BMI. However, obese individuals homozygous for the G-allele showed significantly lower leptin levels (51.4 ± 24 ng/mL) compared to obese patients either heterozygous or homozygous for the A-allele (60.0 ± 26 , $P = 0.02$ after correction for BMI). This result was replicated in an independent population of moderately obese French women. Our study provides further evidence that a defect in the *ob* gene in linkage disequilibrium with the G-allele of

exon 1 might affect leptin levels in obese populations.

Response of leptin levels to short term feeding and fasting in man, influence of circadian cycle. M. Romon, P. Lobel, C. Le Fur, J.L. Edmé, B. Hecquet, J.C. Fruchart, J. Auwerx, J. Dallongeville (Inserm U 325, Institut Pasteur Lille, Service de nutrition CHU, 59045 Lille cedex, France).

Introduction: It has been suggested that leptin levels vary according to a nycthemeral cycle. We hypothesize that this variation could be due to a feeding/fasting cycle. We investigated whether fasting and acute feeding induced changes in circulating leptin levels in humans and whether these changes varied according to a nycthemeral cycle. meal.

Methods: Thirteen healthy subjects (BMI 22.3 ± 1.7 kg/m²) were given either a mixed meal (4.6 ± 0.2 MJ) or remained fasting at night or during the day. Six hours before the beginning of each session, either fed or fasted, they were given the same light meal (2.3 ± 0.8 MJ). Blood samples were drawn at baseline and hourly for 8 h. Leptin response was calculated as the sum of the differences between baseline levels and hourly responses. Comparisons were made by a two-way analyses of variance with repeated measures, followed by the Dunnett test.

Results: Serum leptin levels increased after the test-meal ($+41.8 \pm 38\%$; $P < 0.03$) and decreased in the fasting state ($-29 \pm 15\%$; $P < 0.05$). There were no statistically significant differences in the leptin responses to the test meal between the night and day sessions (40 ± 22 versus $41.8 \pm 38\%$) or to fast (-22 ± 11 versus $-29 \pm 15\%$).

In conclusion, in non-obese subjects, serum leptin levels increased following food intake. This effect was not influenced by nycthemeral cycle.

Photoperiod and nutritional status modulate the expression of the gene encoding leptin in ovine perirenal adipose tissue. M. Bonnet^a, Y. Faulconnier^a, F. Bocquier^a, P. Martin^b, Y. Chilliard^a (^aLaboratoire sous-nutrition des ruminants, Inra, 63122 Saint-Genès-Champanelle; ^bLaboratoire génétique biochimique et cytogénétique, Inra, 78350 Jouy-en-Josas, France).

Leptin, a protein secreted by adipocytes, plays a major role in the regulation of food intake as well as adiposity in rodents and, in addition, modulates their reproductive cycle. Among livestock animals, sheep are one of the more sensitive to photoperiod, which effects both their reproductive cycles as well as their food intake. It was therefore decided to study the respective effects of photoperiod and nutritional status on the expression of the gene encoding leptin in ovine adipose tissue. The experiment was conducted on four groups of five adult, dry, ovariectomized ewes, that were subjected either to a short (S; 8 h/d light) or to a long (L; 16 h/d light) photoperiod, for 3 weeks. Then, all the ewes were underfed (U) to 25 % of their maintenance energy requirements (MER) for 7 days, and half of them were slaughtered (groups S-U and L-U), while the remaining were refed (R) for 14 days at 200 % of MER (groups S-R and L-R). Leptin mRNA level was estimated semi-quantitatively by RT-PCR, and simultaneously the level of cyclophilin transcript was determined as an internal control, because the relevant gene appeared to be invariably expressed. After 28 or 40 cycles of amplification with primers specific to cyclophilin or leptin, respectively, the PCR products were fractionated and visualized on an agarose gel (3 %) stained by ethidium bromide. The leptin signal was increased both by photoperiod ($+65\%$; $P < 0.03$) and refeeding ($+44\%$; $P < 0.10$) and the effects of these two factors were additive (0.89, 1.86, 1.64 and 2.33 in