LEPTIN DIRECTLY STIMULATES PARATHYROID HORMONE SECRETION

Ignacio Lopez[1,2], Carmen Pineda[1,2], Ana Raya[1,2], María E Rodríguez-Ortiz[2], Juan M Díaz-Tocados[2], Rafael Ríos[1,2], Mariano Rodriguez[2], Escolastico Aguilera[1,2] and Yolanda Almadén[2].

[1] Dept. Animnal Medicine and Surgery, Veterinary School, University of Cordoba, Spain.
[2] Research Unit, Nephrology Service, Hospital Reina Sofia, IMIBIC, Cordoba, Spain.

INTRODUCTION

- Leptin is an adipokine secreted by fat tissue which plays a major role in energy metabolism.
- Leptin is best known for its modulatory effects on food intake: by acting on the central nervous system leptin inhibits appetite.
- A relationship between obesity, plasma leptin concentration and primary hyperparathyroidism has been previously reported.

OBJECTIVE

The aim of this study was to test the hypothesis that leptin directly stimulates PTH secretion by the parathyroid glands.

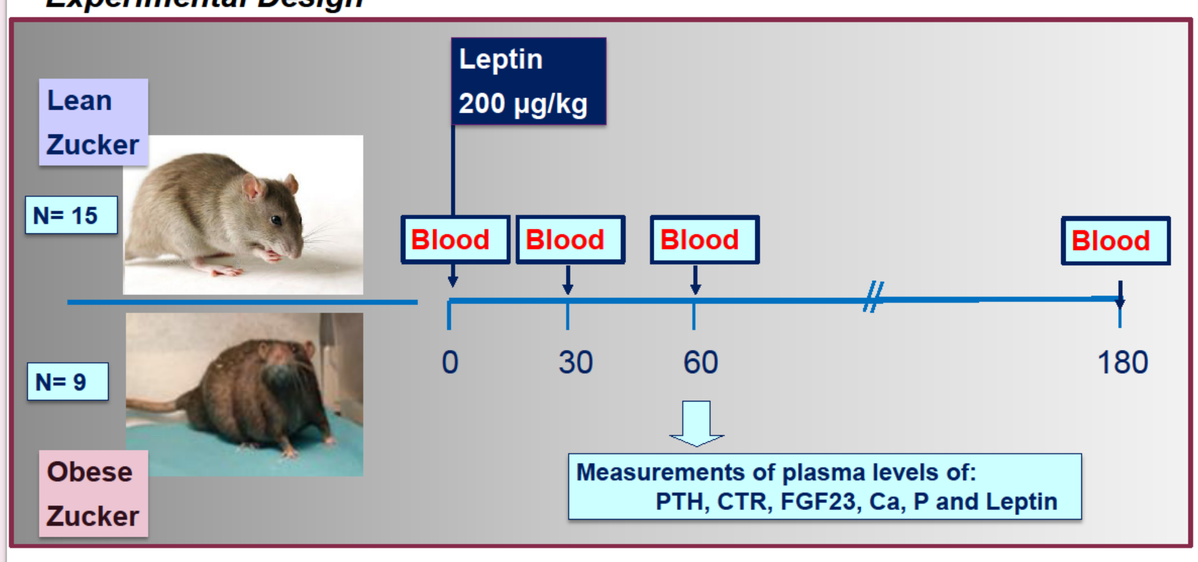
MATERIALS AND METHODS

In vivo studies

Animal Model

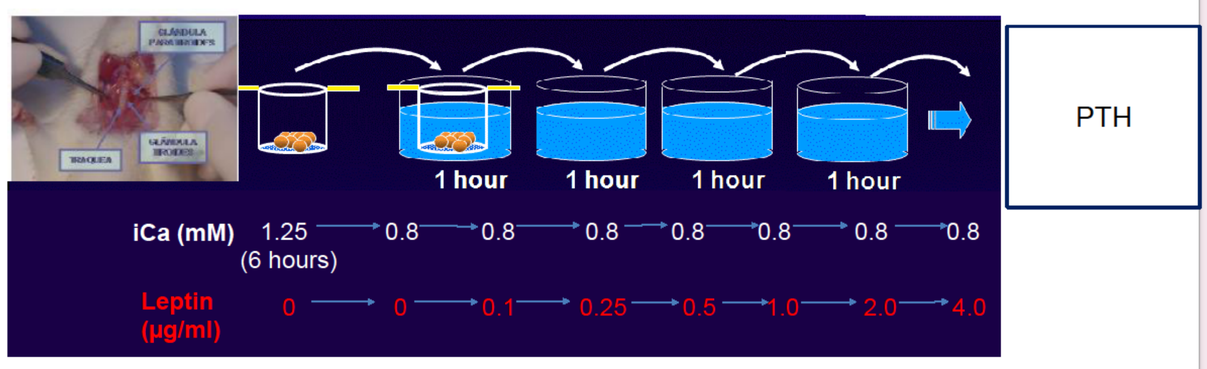
•Two strains of rats were used in the *in vivo* studies: lean (Fa/Fa, Fa/fa) Zucker rats (n=15) and obese (fa/fa) Zucker rats (n=9). The fa/fa Zucker rats are natural mutants that do not express active leptin receptors and therefore are non sensitive to leptin.

Experimental Design



In vitro studies

• Rat parathyroid glands were obtained as previously described (Almaden *et al.* 1996) from male Wistar rats (250 g body wt).



Measurements

- Blood for measurement of **iCa** was performed by selective electrode (Ciba-Corning 634 ISE Ca2+/pH Analyzer, Essex, England).
- Plasma levels of **PTH** were quantified using a rat bioactive intact PTH ELISA kit (Immunotopics, San Clemente, CA, USA).
- Plasma **P** was measured by spectrophotometry (BioSystems SA, Barcelona, Spain).
- Radioimmunoassay was used in plasma samples to determine **leptin** (Millipore, St. Charles, MO, USA) and **1,25(OH)2-vitamin D3** (IDS kit, Boldon, UK).
- Plasma **FGF23** levels were determined using a rat FGF23 ELISA Kit (Kainos laboratories Inc., Tokyo, Japan).

RESULTS

In vivo studies

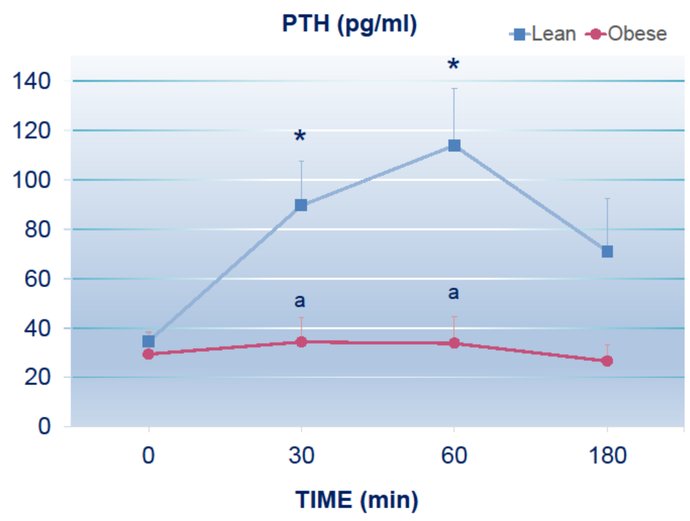


Figure 1: Plasma parathyroid hormone (PTH) concentrations before and after intraperitoneal administration of leptin (200 µg/kg) to six wild type (Fa/Fa or Fa/fa) Zucker rats (LEAN) and to four obese (fa/fa) Zucker rats (OBESE).
***p<0.05 vs time 0. [a]p<0.05 vs Lean at the same time point.**

Table 1: Blood biochemistry before (0 min) and after (60 min) administration of leptin (200 µg/kg ip) to lean and obese Zucker rats

Parameter	Rat	Time (min)	
		0	60
Leptin (pg/mL)	Lean	4.85 ± 1.9	104.2 ± 31.0*
	Obese	13.3 ± 0.1	87.3± 36.2*
PTH (ng/mL)	Lean	52.8± 6.9	166.9 ± 42.9*
	Obese	61.2 ± 18.6	62.8± 17.8
iCa (mmol/L)	Lean	1.10± 0.03	1.08± 0.02
	Obese	1.13± 0.1	1.19± 0.02
P (mg/dL)	Lean	4.7± 0.1	5.0± 0.2
	Obese	6.2± 0.5	5.7± 1.0
$1,25(OH)_2D_3$ (mg/dL)	Lean	96.5± 19.5	91.9± 21.5
	Obese	15.3 ± 10.2	16.6± 8.9
FGF 23 (pg/mL)	Lean	401.8 ±16.7	421.7± 119.0
	Obese	625.3± 235.0	648.8± 267.0

In vitro studies

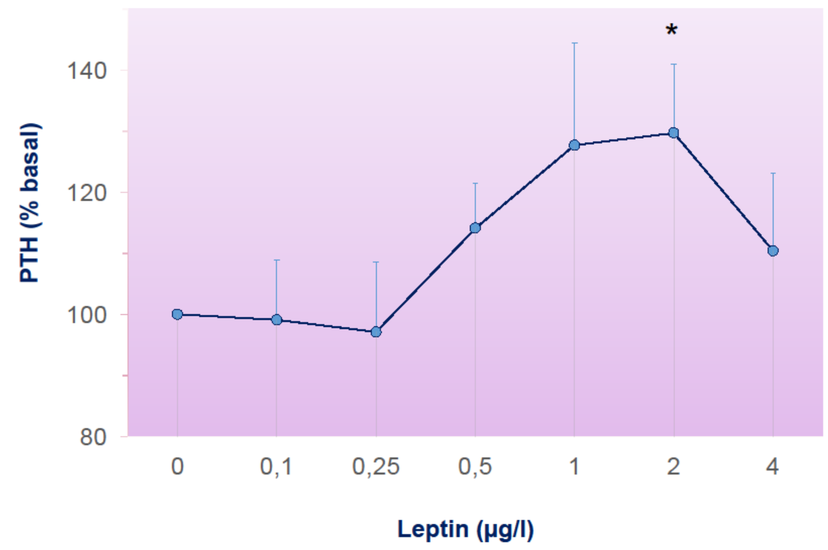


Figure 2: Parathyroid hormone secretion (PTH) by cultured rat parathyroid glands incubated with calcium = 0.8 mM in response to increasing concentrations of leptin.*p<0.05 vs basal.

CONCLUSION

The results of the present study demonstrate a direct stimulatory effect of leptin on PTH secretion and suggest the existence of an endocrine axis between fat tissue, where leptin is mainly produced, and the parathyroid glands.

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