

Growth Processes for a pulse of leptin in fasting human subjects

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Abstract

A meal-like transient hyperinsulinemia and hyperglycemia, with a pulse of xamethasone, increased serum leptin levels from baseline by $54\pm 21\%$ at 9 h ($P = 0.038$). In the absence of transient hyperglycemia, leptin increased significantly after doses of both insulin and xamethasone. The effect of insulin was dose-dependent, with a larger increment of serum leptin at 9 h after the highest dose of insulin ($75.2\pm 15.7\%$ vs $21.3\pm 8.5\%$, $P = 0.013$). Fasting, with or without dexamethasone, resulted in a significant 20% decrease in leptin from morning basal levels. Conversely, the administration of a pulse of insulin and glucose, in the absence of dexamethasone, prevented the drop in serum leptin observed during fasting, regardless of the insulin dose or the serum glucose elevation. The permissive effect of dexamethasone, a single pulse of insulin triggered a rise in serum leptin in humans, even in the absence of transient hyperglycemia. A single pulse of insulin with glucose can prevent the drop in serum leptin normally observed during fasting. We also find the Growth Processes of Leptin

Keywords: GC Processes, Leptin, Glucocorticoids, Cycle length

I. Introduction

Leptin, the peptide hormone secreted by the fat cells, is secreted in proportion to fat mass (1) as well as regulated by nutritional (2,3) and hormonal factors, such as glucocorticoids and insulin. Glucocorticoids and insulin have both been shown to be part of leptin regulation. Oral administration of dexamethasone at doses varying from 1.5 to 6 mg per day increases serum leptin in humans (4). We have shown that this effect is dependent on food intake. A pulse of dexamethasone followed by three meals stimulated leptin by 100% at 10 h. In contrast, the administration of dexamethasone did not increase leptin levels in fasted subjects. The factors related to food intake (gastrointestinal hormones, insulin and/or glucose or other nutrients) that synergize with dexamethasone to increase leptin are unknown. Twenty-nine subjects (25 males, 4 females), mean age 26 ± 5 years, were studied. They were all healthy, non-smokers, non-obese (body mass index = 25 ± 2 kg/m²), with a normal physical examination, routine blood work and thyroid function tests, taking no medication, not depressed as assessed by the Beck questionnaire with an oral glucose tolerance test within the normal range, and a stable body weight for at least 3 months prior to the study. Total body fat (mean $21\pm 6\%$) was measured by DEXA scan. Their baseline glucose, insulin and leptin levels were respectively 5.1 ± 0.4 mmol/l, 71 ± 29 pmol/l and 5 ± 4 ng/ml. The study protocols were approved by the Institutional Review Board of St Luke's/Roosevelt Hospital, and informed written consent was obtained prior to inclusion in the study

II. Methods

The rises in glucose and insulin, shown in Fig. 1, followed the same pattern as those observed after food intake in our previous experiments (9). The peak increases in serum glucose were 8.5 ± 0.6 mmol/l and 8.6 ± 0.5 mmol/l, with and without dexamethasone respectively ($P = 0.905$), levels similar to the one seen in our previous meal studies. Peak serum insulin levels were 279 ± 49 pmol/l and 382 ± 52 pmol/l respectively. In previously published experiments, insulin levels peaked at 450 pmol/l after a breakfast and 4 mg dexamethasone and at 600 pmol/l after a 1700 kcal meal and 2 mg dexamethasone. Plasma insulin and C-peptide (expressed as peak values and AUC) and plasma glucose (expressed as peak values) were not significantly different between the two conditions (with and without dexamethasone). When given together with dexamethasone, a pulse of insulin and transient rise in glucose resulted in an increase in serum leptin at 9 h ($54\pm 21\%$ above baseline, $P = 0.038$), with a significant effect starting 6.5 h after treatment (Fig. 1). The AUC for FFA was significantly higher in the insulin plus dexamethasone condition than in the insulin-only condition (73 ± 24 vs 44 ± 18 mmol/l per 9 h, $P = 0.015$). The administration of insulin resulted in a decrease in FFA levels from baseline for 5 h, followed by a subsequent increase in FFA levels to baseline. In the insulin plus dexamethasone condition, the suppressing effect of insulin on FFA was shorter, about 2 h, after which FFA levels increased to reach levels 44% higher than the insulin-only condition, indicating a lipolytic effect of dexamethasone. The effect of dexamethasone on leptin persisted after adjustment for FFA changes.

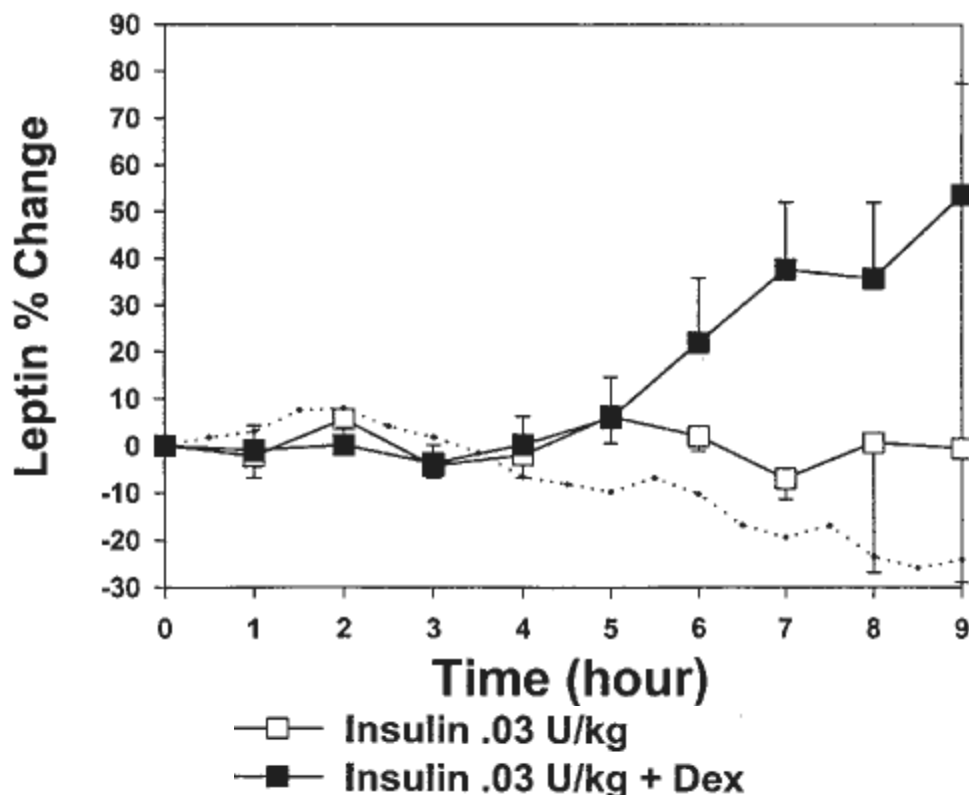


Figure: ‘meal-like’. Changes over time in leptin levels after administration of a pulse of insulin with or without dexamethasone (Dex), in the presence of a transient rise in glucose ($n = 8$). The dotted line represents the change in serum leptin under fasting conditions ($n = 9$).

III. Mathematical model:

Considered GC processes where the inflow to the system is constant and the timing of crashes and the crash magnitude depend on the state of the system and we consider a class of state-dependent GC processes which go back to their initial states after the crashes. They grow according to a discrete-time random walk with nonnegative increments between crash times at which they collapse to 0. It is assumed that the probability of crashing depends on the level of the process[6,7].

The GC process $(X_t)_{t \geq 0}$ is a homogeneous Markov chain with a transition rule corresponding to a mixture of discrete and continuous distributions:

$$P(X_t = 0 / X_{t-1} = x_{t-1}) = 1 - \phi(x_{t-1}), \quad x_{t-1} \geq 0$$

$$P(X_t \in (x_t, x_t + dx_t) / X_{t-1} = x_{t-1}) = \phi(x_{t-1})f(x_t - x_{t-1})dx_t, \quad x_t \geq x_{t-1}$$

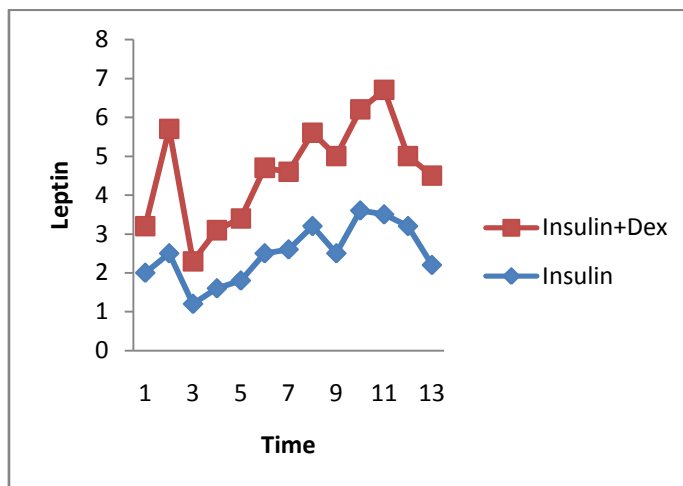
Therefore, the stationary distribution, if it exists and is unique, has a point mass k at $\{0\}$ and a probability density function l on $(0, \infty)$. They satisfy the conditions

$$K = \int_0^{\infty} 1 - \Phi(x)l(x)dx, \quad l(x) = kf(x) + \int_0^x \Phi(y)f(x-y)l(y)dy.$$

The atom $\{0\}$ is regenerative and can be used to define the following regeneration times: $T_0 = 0$ and $T_n = \inf\{t > T_{n-1} : X_t = 0\}$, $n \geq 1$. In this way the GC Markov chain split up into independent, identically distributed cycles $(X_t)_{T_n \leq t < T_{n+1}}$, $n \geq 1$. We denote the independent, identically distributed cycle lengths by $D_n = T_{n+1} - T_n$, $n \geq 1$. Finally we define the monotonically decreasing sequence $(P_n)_{n \geq 0}$ by $P_0 = 1$ and

$$P_n = E \left[\prod_{k=1}^n \Phi(s_k) \right], n \geq 1,$$

Therefore, $p_n = 0.2316$



IV. Conclusion

The administration of a pulse of insulin and glucose, in the absence of dexamethasone, prevented the drop in serum leptin observed during fasting, regardless of the insulin dose or the serum glucose elevation. The permissive effect of dexamethasone, a single pulse of insulin triggered a rise in serum leptin in humans, even in the absence of transient hyperglycemia. A single pulse of insulin with glucose can prevent the drop in serum leptin normally observed during fasting. We also find the Growth Processes of Leptin

References

- [1] Considine RV, Sinha MK, Heiman ML, Kriauciunas A, Stephens TW, Nyce MR, et al. *Serum immunoreactive-leptin concentrations in normal-weight and obese humans*. New England Journal of Medicine 1996;334:292–295. [PubMed: 8532024]
- [2] Boden G, Chen X, Mozzoli M, Ryan I. *Effect of fasting on serum leptin in normal subjects*. Journal of Clinical Endocrinology and Metabolism 1996;81:3419–3423. [PubMed: 8784108]
- [3] Kolaczynski JW, Ohannesian JP, Considine RV, Marco C, Caro JF. *Response of leptin to short-term and prolonged overfeeding in humans*. Journal of Clinical Endocrinology and Metabolism 1996;81:4162–4165. [PubMed: 8923877]
- [4] Miell JP, Englaro P, Blum WF. *Dexamethasone induces an acute and sustained rise in circulating leptin levels in normal human subjects*. Hormone and Metabolic Research 1996;28:704–707. [PubMed:9013746]
- [5] Kiess W, Englaro P, Hanitsch S, Rascher W, Attanasio A, Blum WF. *High leptin concentrations in serum of very obese children are further stimulated by dexamethasone*. Hormone and Metabolic Research 1996;28:708–710. [PubMed: 9013747]
- [6] Marshall, A.W. and Shaked, M., “New better than used processes”, *Adv. Appl. Proba.*, **15** (1983), 601-615
- [7] Shanthikumar, J.G. and Sumita, U., “General shock models associated with correlated renewal sequences”, *J. Appl. Proba.*, **20** (1983), 600-614