

## Leptin-induced decrease in food intake in chickens

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Received 22 September 1999; received in revised form 10 November 1999; accepted 20 December 1999

### Abstract

The effect of intracerebroventricular (i.c.v.) injection of leptin was investigated using broiler and Single Comb White Leghorn (SCWL)-type chickens. These represent relatively fast- and slow-growing birds, respectively. The i.c.v. injection of leptin decreased food intake in both broilers and Leghorns in a dose-dependent manner. The most efficacious dose appeared to be 10  $\mu\text{g}$  in both types of chickens. Water intake was generally not affected by leptin, indicating that this effect was not due to general malaise. It appears that leptin can act within the central nervous system of birds to decrease food intake. © 2000 Elsevier Science Inc. All rights reserved.

**Keywords:** Leptin; Food intake; Water intake; Chickens

### 1. Introduction

It has been known for years that endogenous lipid stores are well regulated [20]. Although it is unlikely that such regulation can be explained by a single gene, the cloning of the *ob* gene encoding for leptin has shed some light on mechanisms regulating lipid deposition [29]. In mammals, it appears that mutations in either leptin [23] or its receptor [8,22] results in changes in lipid stores and food intake.

Leptin is thought to act as a signal between the peripheral lipid stores and the central nervous system [7], gaining access to the brain at the arcuate nucleus and choroid plexus by a specific transport system [3]. Intracerebroventricular (i.c.v.) or intrahypothalamic injections of leptin have been reported to decrease food intake in a variety of mammals including mice [8], rats [9], pigs [4], and monkeys [26]. Leptin probably acts by altering neuropeptide Y expression and release from neurons originating in the arcuate nucleus [24,27].

The gene encoding leptin in chickens has recently been cloned [2,25]. Unlike in mammals, the gene is expressed not only in adipose tissue, but also in liver. Interestingly, both adipose tissue [21] and liver [19] are believed to be peripheral sites involved in food intake regulation.

It is well documented that the modern broiler and Leghorn are relatively fast-growing and slow-growing, respec-

tively [5]. It has been shown that the mechanisms regulating food intake differ between Leghorns and broilers, presumably because of differential genetic selection for growth rate [10]. It is reasonable to expect that a signal originating from adipose or hepatic tissue would act similarly in birds and mammals. Recently, however, it was reported that i.c.v. injections of leptin did not reduce food intake in young chickens [6]. The purpose of the present study was to determine if leptin acts within the central nervous system of chickens to alter food intake in two types of chickens differing in growth rate.

### 2. Materials and methods

#### 2.1. Animal preparation

Broiler and Leghorn cockerels obtained on the day of hatch were reared in heated batteries with raised wire-bottom floors until 4, and 7 weeks of age, respectively. Thereafter, they were moved to individual cages. Broilers have been selected for rapid body weight gain [13], whereas Leghorns have been indirectly selected for slow growth [16]. These ages were selected so that the birds would be of similar weight at the time of the experiments. A mash diet (20% crude protein, 2864 kcal/kg metabolizable energy) and water were provided ad lib consumption, and lighting was continuous.

After being moved to individual cages, each bird was anaesthetized with sodium pentobarbital (25 mg/kg), and a 23-gauge thin-walled stainless steel guide cannula was stereotaxically implanted into the right lateral ventricle as de-

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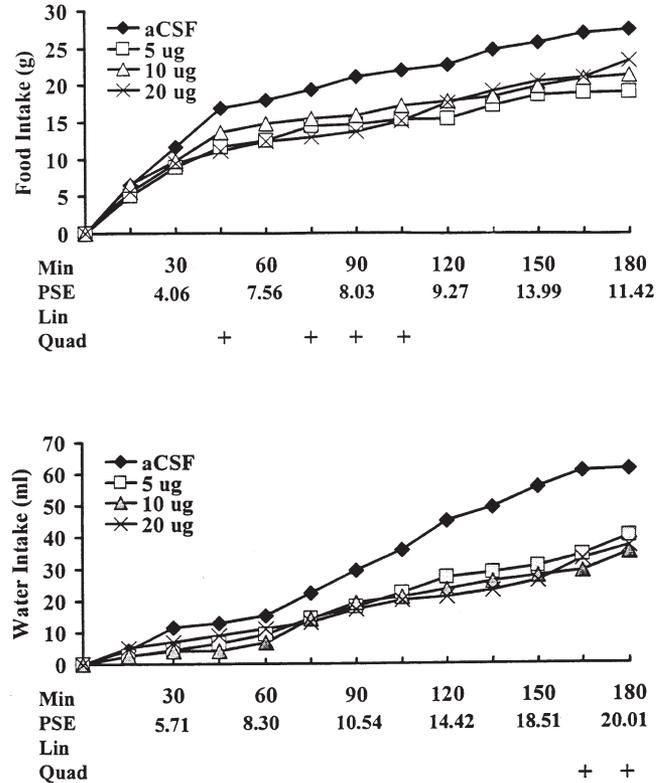
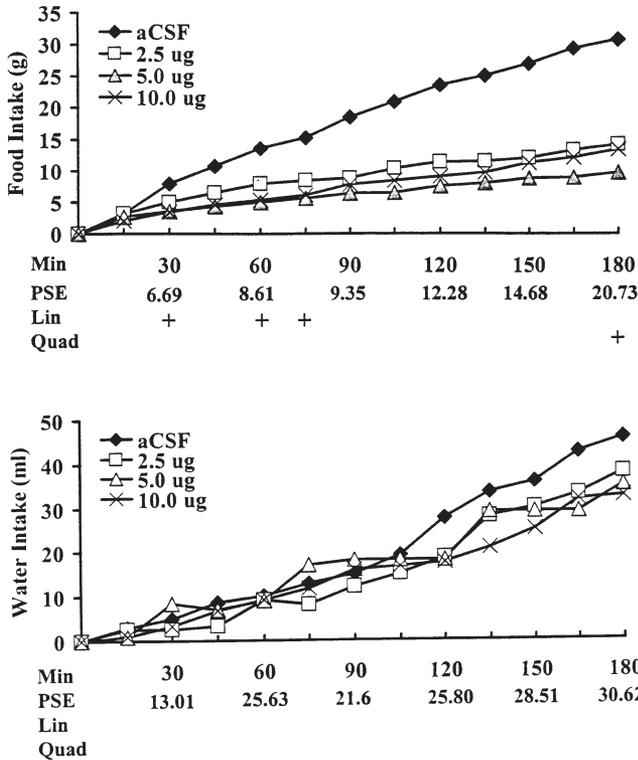


Fig. 1. Cumulative food and water intake of male Single Comb White Leghorns following intracerebroventricular injection of 0–10 µg human recombinant leptin. Lin, linear contrast; Min, minutes; PSE, pooled standard error; Quad, quadratic contrast;  $^+p \leq 0.05$ .

Fig. 2. Cumulative food and water intake of male Single Comb White Leghorns following intracerebroventricular injection of 0–20 µg human recombinant leptin. LIN, linear contrast; Min, minutes; PSE, pooled standard error; QUAD, quadratic contrast;  $^+p \leq 0.05$ .

scribed by Denbow and Van Krey [11]. Placement in the ventricle was verified by the presence of cerebrospinal fluid in the guide cannula. Birds were allowed a minimum of 3 days recovery before beginning injections.

2.2. Experiment 1

Eight Leghorn cockerels were used in a replicated Latin square design with birds and days as blocking factors. All solutions were made in artificial cerebrospinal fluid (aCSF; [1]), which served as the control. The aCSF was filtered through a 0.22-µm filter (Gelman Instrument Co., Ann Arbor, MI) prior to injection. The birds were injected with 0–20 µg of human recombinant leptin (Calbiochem, La Jolla, CA) in a volume of 10 µL. The chicken leptin gene shows 83% homology with human gene [2,25]. Injections were made using a 27-gauge stainless-steel cannula connected to a 10-µL Hamilton syringe with a 60-cm length of PE-20 tubing (Clay Adams). Food and water intake were monitored at 15-min intervals through 3 h postinjection. Intake was again determined at 24 h postinjection to determine if there was a carry over effect of the drug.

2.3. Experiment 2

This experiment was similar to the previous experiment except that broilers were used.

2.4. Analysis

Cumulative food and water intake were analyzed using analysis of variance at each time period. Treatment effects were partitioned into linear and quadratic contrasts to determine the dose–response relationships at each time period. Significance implies  $p \leq 0.05$ .

3. Results and discussion

The i.c.v. injection of human recombinant leptin decreased food intake in both Leghorn and broiler type chickens (Figs. 1–4). It appeared that 10 µg was the most efficacious dose. These results support those found in other species in which injections both inside or outside the blood–brain barrier reduced food intake [4,7,14,15,22]. The site of action in which leptin is working within the central nervous system of birds has not been identified. However, it appears likely that the site is similar to that in mammals where leptin acts at the arcuate nucleus to alter neuropeptide Y expression [27]. Neuropeptide Y stimulates feed intake in birds similarly to that in mammals [12,18], and has also been shown to be localized within the hypothalamus [17].

Water intake was generally not altered by the i.c.v. injection of leptin (Figs. 1–4). The only significant effect on water intake was observed at 165 and 180 min following the

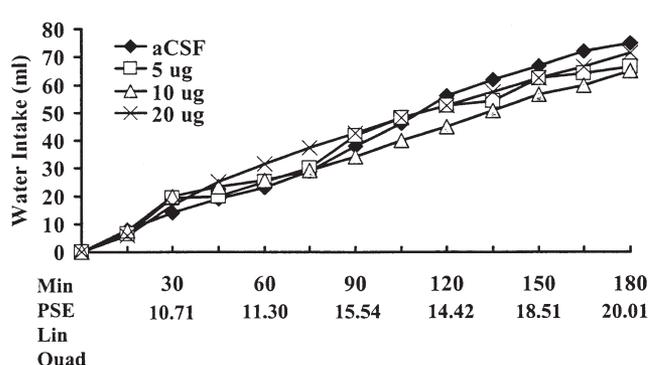
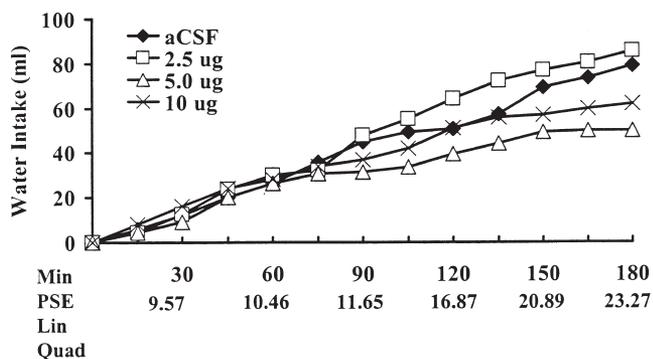
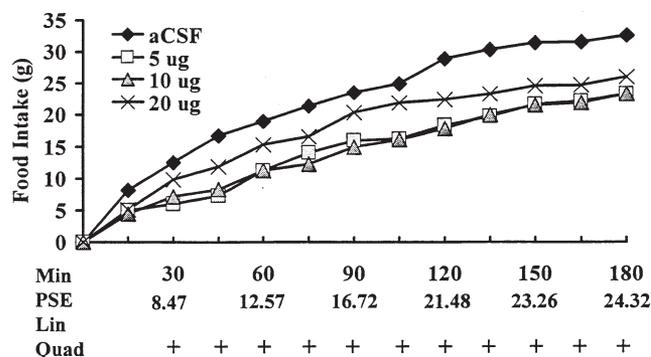
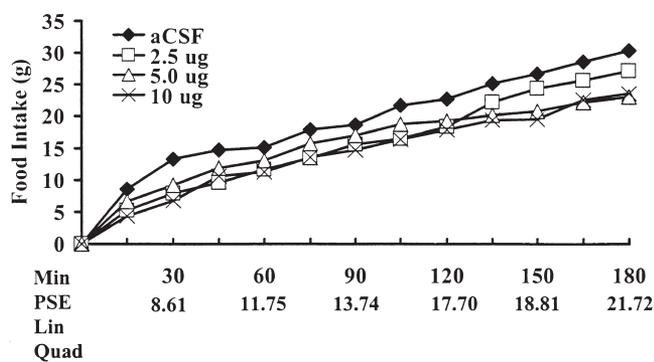


Fig. 3. Cumulative food and water intake of broilers following intracerebroventricular injection of 0–10  $\mu$ g human recombinant leptin. Lin, linear contrast; Min, minutes; PSE, pooled standard error; Quad, quadratic contrast;  $^+p \leq 0.05$ .

Fig. 4. Cumulative food and water intake of male broilers following intracerebroventricular injection of 0–20  $\mu$ g human recombinant leptin. Lin, linear contrast; Min, minutes; PSE, pooled standard error; Quad, quadratic contrast;  $^+p \leq 0.05$ .

i.c.v. injection of leptin at the higher doses in Leghorns (Fig. 2). Because food intake was decreased within 45 min of leptin injection in the same experiment, the effect on water intake was probably an indirect effect of the decreased food intake. The i.c.v. administration of leptin has been shown to decrease food intake in both lean and obese rats [28].

The sensitivity of the brain to leptin appears to be related to the animal's genetic background. Wang et al. [28] reported that both lean and obese Zucker rats responded to i.c.v. leptin. However, Halass et al. [15] found that  $A^y$  mice were relatively unresponsive to i.c.v. leptin compared to lean mice. In the present study, both broilers and Leghorns were responsive to the anorexigenic effects of i.c.v. leptin.

The results of the present study differ from those of Furuse et al [12], who reported that i.c.v. injection of mouse leptin had no effect on food intake in 2-day-old broilers of SCWL. Although the reason for these disparate results is unclear, it may be due to either age or source of leptin.

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