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Leptin, body composition, adrenal and gonadal hormones among captive male baboons

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Abstract: Morphometric and hormonal measures were collected from 21 captive savanna baboons (*Papio cynocephalus*) maintained at the Tulane National Primate Research Center in order to determine age-related patterns in leptin levels over the life course as well as their relationships to body composition and adrenal and gonadal steroids. Comparison of leptin levels between peri-pubertal, adolescent, young adult, and fully mature males show lower levels among adolescent as compared with young adult males ($P = 0.05$ by Kruskal–Wallis ANOVA). In addition, abdominal fat varied among age groups ($P = 0.003$ by Kruskal–Wallis ANOVA) with the peri-pubertal animals lower than the adolescents, young adults, and prime adults. However leptin was not related to any measure of body composition, including abdominal fat, or to adrenal hormones (dehydroepiandrosterone, dehydroepiandrosterone-sulfate, and cortisol) or gonadal hormones (testosterone and estradiol). Age-related changes in leptin appear similar to those reported for captive rhesus macaques, while the failure to find an association between leptin and abdominal fat is interestingly different. These results confirm elevated levels of leptin in captive baboons compared with their wild counterparts and suggest that they result from changes in fetal development.

Key words: abdominal fat – *Papio cynocephalus* – skinfolds

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Introduction

Since it was first reported, leptin has attracted much attention as a signal of energetic status [5]. However, levels among humans and mice, the most common subjects of leptin research may be un-naturally elevated due to high levels of obesity [2], and hence provide misleading information about the function of leptin. It has been suggested that in the natural condition, leptin is not an all-purpose indictor of energetic status, but rather acts as a threshold marker of adequate energy stores [8, 19].

In support of this position, Banks et al. [2] reported much lower levels of leptin in wild male baboons as compared with captive counterparts. The captive animals exhibited much higher leptin to weight ratios suggesting that increased adiposity was responsible for their increased leptin levels. Furthermore, leptin levels were highest in the young captive animals and declined with age while wild animals showed no apparent change with age, implying that the age-related decline in leptin was related to declining adiposity.

However, the oldest animal in Banks et al.'s sample was 5 years old (estimated on dental development), just about the beginning of reproductive maturation, limiting any conclusions to the juvenile stage, prior to changes in leptin associated with puberty among both rhesus macaques [21] and humans [7]. In addition, Banks et al. did not specifically measure adiposity. Abdominal adiposity has been related to leptin in other primates [9] and hence might help explain differences in both overall levels and age pattern of leptin among captive and wild baboons.

In order to develop a more complete picture of leptin over the life cycle of captive baboons, we measured leptin in a sample of 21 male savanna baboons, including peri-pubertal, adolescent, and adult individuals. We also obtained morphometric measures, including skinfolds, to look directly at the relationship of adiposity and leptin, as well as adrenocorticol and gonadal hormones to investigate the potential impact of reproductive maturation on leptin.

Materials and methods

This cross-sectional survey utilizes 21 hybrid male baboons between 1.7 and 13.2 years of age maintained at the Tulane National Primate Research Center, Covington, LA, USA. These animals represent all males over 1.7 years of age in a hybrid breeding colony of approximately 330 savanna baboons (sex ratio of males to females, 1:12) of both Olive (*Papio cynocephalus anubis*) and Yellow (*P. cynocephalus cynocephalus*) phylogenetic heritage. All animals were housed in a single 2-acre outdoor corral, a semi-natural ecological context that accommodates normal physical and social activity [17]. Animals were provisioned with Purina Monkey Chow (Ralston Purina Co., St Louis, MO, USA) daily. Diet was supplemented with fresh fruit weekly and water was available *ad libitum*. Matrilineal data and precise chronological ages were maintained in the Center's computer system.

All measurements took place during the population's semi-annual health inspection in early December, 1999. In order to minimize inter-observational error, morphometric measurements and hormonal analyses were made by one investigator (MPM) when possible. However, some morphometric measurements (<20%) were made by another trained investigator. All animals were anesthetized with ketamine hydrochloride (10 mg/kg), a dissociative anesthetic widely used in studies requiring transient animal tranquilization [4]. Ketamine has shown no significant effects on serum androgen levels or production rates [24]. Each animal was examined once, between 07:00 and 09:00 hours to eliminate any circadian effect. A complete description of the anthropomorphic measurements can be found in Muehlenbein et al. [11, 10]. In brief, body weight, length, upper arm circumference, abdominal and hip circumferences as well as tricep, periumbilicular (abdominal), and subscapular skinfolds were obtained.

A blood sample was collected from the femoral vein using a 10-ml SST Vacutainer Collection Tube (Beckton-Dickson, Franklin Lakes, NJ, USA) and a 21-gauge needle. These blood samples were collected immediately following tranquilization, limiting gonadal and adrenal hormone concentrations from being significantly influenced by the stress of capture [18]. The sera from the blood collected was aliquoted into two containers and frozen at −40°C until assayed for estradiol, total testosterone, dehydroepiandrosterone-sulfate (DHEA-S), dehydroepiandrosterone (DHEA), and cortisol using solid-phase radioimmunoassay (RIA) procedures (estradiol/testosterone/DHEA-S: Diagnostic Products Corp., LA, USA; DHEA/cortisol: Diagnostic Systems Laboratory, Webster, TX, USA). Intra-assay coefficients of variation were <5.9% for all assays. Leptin levels were determined using a non-human primate-specific RIA kit by Linco Research, Inc. (St Charles, MO, USA).

Due to the small sample size ($N = 21$), normal distribution of variables with equal variances across the relatively wide age range cannot be assumed. Thus, the morphometric and hormonal parameters of the four age groups of animals used here were analyzed and compared via non-parametric statistics using Statistica for Windows [20]. The Kruskal–Wallis one-way analysis of variance by ranks was used to assess overall significance. To compare individual groups with one another, the Mann–Whitney *U*-test was utilized. Partial correlations controlling for age were used to test the relationship of leptin to body composition and hormone measures. For all statistical tests, alpha was set at $P < 0.05$. One leptin value was considered an outlier and removed from the analysis, resulting in a sample size of 20.

Results

The average overall level of leptin for this sample of male baboons was (2.37 ± 0.39 ng/dl), comparable with levels reported by of Banks et al. for their sample of 17 captive baboons [2].

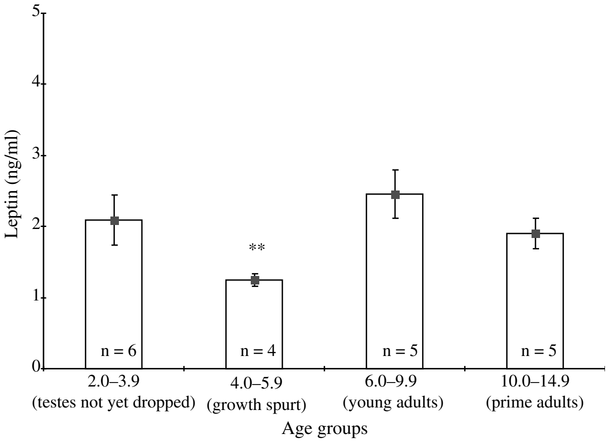

Fig. 1. Age-related changes in leptin levels in baboons by age groups. Average leptin levels (±SEM) by categories corresponding to the major phases of the baboon life cycle. '**' Represents a marginally significant difference between adolescents (1.25 ± 0.09 ng/ml) and young adults (2.46 ± 0.34 ng/ml) ($P = 0.05$) as determined by Kruskal–Wallis ANOVA.

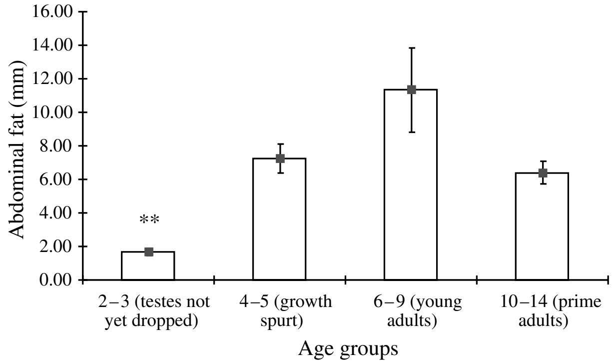

Fig. 2. Age-related changes in abdominal fat levels in baboons by age groups. Average abdominal fat levels (±SEM) by categories corresponding to the major phases of the baboon life cycle. Kruskal–Wallis ANOVA indicates statistically significant overall difference between groups ($P = 0.003$). '**' Represents a significant difference between peri-pubertal males and each of the other three age groups ($P < 0.01$ vs. adolescents; $P < 0.002$ vs. young adults; $P < 0.001$ vs. older adults) as determined by Mann–Whitney *U*-test.

Figure 1 shows the pattern of leptin by age group. Overall there was a non-significant trend toward differences in leptin levels across the age groups ($P = 0.09$), with the young adults exhibiting the highest levels and adolescents the lowest. In group contrasts, the adolescents (1.25 ± 0.09 ng/ml) had marginally lower leptin levels compared with the young adults (2.46 ± 0.34 ng/ml) ($P = 0.05$).

Figure 2 shows the pattern of periumbilicular skinfold by age group. Overall there was a highly significant difference ($P = 0.003$) between groups with the peri-pubertal animals lower than the other three groups. Group contrasts indicate that the peri-pubertal males had significantly smaller periumbilicular skinfolds than all the other groups. None of the other group comparisons showed significant differences.

Table 1 shows the partial correlations between leptin and measures of body composition and hormones, controlling for age. Leptin is not related to any measure of body composition, including abdominal fat. Nor is leptin related to either the gonadal (testosterone and estrogen) or adrenocortical (DHEA, DHEA-S, and cortisol) hormones measured.

Table 1. Correlations[1] of variables to leptin among baboons

Age (years)	0.1551
Weight (kg)	0.1334
Length (cm)	−0.0894
PMI[2] (kg/m^2)	0.1822
Tricep fat (mm)	−0.0800
Subscapular fat (mm)	0.1535
Abdominal fat (mm)	0.1464
Tricep circumference (cm)	−0.0188
Waist circumference (cm)	0.1503
Testosterone (ng/ml)	0.1191
Estradiol (pg/ml)	−0.2185
Cortisol (μg/dl)	−0.0084
DHEA[3] (ng/ml)	−0.2215
DHEA-S[4] (μg/dl)	−0.0986

[1]Partial correlation coefficients when controlling for age.
[2]Primate mass index.
[3]Dehydroepiandrosterone.
[4]Dehydroepiandrosterone-sulfate.

Discussion

The results reported here are important in raising questions about the age-related patterns of leptin in captive baboons and their significance for understanding the role of leptin in human reproductive maturation. The leptin levels reported are similar to those of Banks et al., supporting the conclusion that leptin levels in captive baboons are elevated relative to their wild counterparts [2]. Yet, our findings suggest that declines in leptin levels with age among captive baboons are restricted to juvenile animals with increased levels among young adults paralleling increased abdominal fat. The overall age pattern of leptin is consistent with earlier reports that leptin levels decline in captive juvenile macaques prior to puberty as growth rates decline and then increase during puberty [21].

However, our failure to find a significant relationship between leptin and body composition, particularly abdominal fat contrasts with previous findings among captive rhesus and pigtail macaques [9], suggesting that abdominal fat may not be as important an adipose depot among baboon males as it is as among macaques. Other observers have noted the very low percentage of body fat on baboon males [1, 16].

Coelho et al. reported increasing adiposity among olive baboons from birth to age 8, contrary to declining leptin levels [6]. Instead, declines in leptin among juvenile male baboons may be understood in light of recent findings that leptin is related to placental function and fetal growth in both baboons [12] and humans [3, 14]. Furthermore, among humans, placental cord leptin has been related to BMI [15] and birthweight [13]. Thus increased nutritional status among captive baboon mothers relative to their wild counterparts may lead to increased levels of both adipose tissue and leptin in neonates, which in turn decline with age prior to reproductive maturation. However, wild baboons show very little change in leptin prior to reproductive maturation [2].

The resulting picture of age-related changes of leptin in baboon males contrasts with that of human males for whom leptin levels increase prior to puberty and then decline with puberty [7]. This contrast suggests different relationship of energetics and pubertal growth between the two species with human males accumulating fat in order to support the adolescent growth spurt [22, 23] and baboon males showing no decrease in adiposity as part of pubertal maturation. Further research is required to determine if increased adiposity and leptin in captive adult male baboons constitute the effects of captivity or represent fundamental differences in the role of energetics in pubertal development among baboon and human males.

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