ELSEVIER

Comparative Biochemistry and Physiology Part A 129 (2001) 887–895

CBP

www.elsevier.com/locate/cbpa

Concentrations of insulin-like growth factor-I in adult male white-tailed deer (*Odocoileus virginianus*): associations with serum testosterone, morphometrics and age during and after the breeding season

Stephen S. Ditchkoff[a,*], Leon J. Spicer[b], Ronald E. Masters[c], Robert L. Lochmiller[a,✠]

[a] *Department of Zoology, Oklahoma State University, Stillwater, OK 74078, USA*
[b] *Department of Animal Science, Oklahoma State University, Stillwater, OK 74078, USA*
[c] *Department of Forestry, Oklahoma State University, Stillwater, OK 74078, USA*

Received 18 July 2000; received in revised form 2 March 2001; accepted 6 March 2001

Abstract

Our understanding of insulin-like growth factor-I (IGF-I) in cervids has been limited mostly to its effects on antler development in red deer (*Cervus elaphus*), roe deer (*Capreolus capreolus*), fallow deer (*Dama dama*), and pudu (*Pudu puda*). Although IGF-I has been found to play a critical role in reproductive function of other mammals, its role in reproduction of deer is unknown. The objectives of the present study were to determine if serum levels of IGF-I change during the breeding season, assess whether age influences serum IGF-I, compare levels of IGF-I measured during and following the breeding season, and determine if IGF-I is associated with body and antler characteristics in free-ranging adult, male white-tailed deer (*Odocoileus virginianus*). We collected serum and morphometric data from hunter-harvested and captured white-tailed deer to investigate these objectives. Mean level of serum IGF-I during the breeding season was 63.6 ng/ml and was greatest in deer between 2.5 and 5.5 years old (57.4–79.9 ng/ml). Levels of serum IGF-I decreased by approximately 40% as the breeding season progressed, but levels were less in deer following the breeding season (34.6 ng/ml). Both body and antler size were associated positively with IGF-I when controlling for age. Serum testosterone was also associated positively with IGF-I. Levels of serum testosterone during the breeding season generally increased with age from 4.82 (1.5 years old) to 18.79 ng/dl (5.5 years old), but decreased thereafter. These data suggest that IGF-I may be an important hormone in breeding, male white-tailed deer.

Keywords: Age effects; IGF-I; Male; *Odocoileus virginianus*; Seasonality; Testosterone; White-tailed deer

* Corresponding author. Present address: School of Forestry and Wildlife Sciences, Auburn University, AL 36849, USA. Tel.: +1-334-844-9240; fax: +1-334-844-1084.
E-mail address: ditchss@auburn.edu (S.S. Ditchkoff).
✠ Deceased.

1095-6433/01/$ - see front matter
PII: S1095-6433(01)00351-8

1. Introduction

Insulin-like growth factor-I (IGF-I) is a 7.5-kDa hormone that is regulated by growth hormone and is functionally similar to proinsulin (Froesch et al., 1985; Rechler and Nissley, 1985; Jones and Clemmons, 1995). In addition to its metabolic effects, IGF-I has been implicated to play an important role in reproduction of numerous species because of its effects on gonadal steroidogenesis (Lin, 1995; Spicer and Echternkamp, 1995; Lin et al., 1998). By acting on Leydig cells, IGF-I directly stimulates gonadotropin-induced testosterone formation (Lin et al., 1986; Lin, 1995; Le Roy et al., 1999) and potentially influences reproductive behavior and success. Although production of testosterone, the most common androgenic hormone in male deer, has been linked to IGF-I secretion (Horikawa et al., 1989; Adam et al., 1995), the relationship between IGF-I and testosterone levels during the breeding season in male deer has not been determined.

While antlers and body size are important determinants of breeding success in male cervids (Clutton-Brock et al., 1982), the importance of testosterone in driving behavioral changes such as aggressiveness cannot be underestimated. Ultimately, IGF-I may indirectly influence breeding success in male cervids via its influence on circulating levels of testosterone and subsequent effects on behavior (Bartoš et al., 1998). In captive reindeer, systemic concentrations of IGF-I peaked during the rut (Bubenik et al., 1998), however, in another captive cervid, the pudu (*Pudu puda*), seasonal concentrations of IGF-I in males were at a minimum during the breeding season (Bartoš et al., 1998). A positive relationship between serum concentrations of IGF-I and antler growth in captive roe deer (*Capreolus capreolus*; Schams et al., 1992) and fallow deer (*Dama dama*; Bartoš et al., 2000) has been reported. However, changes in IGF-I concentrations during the breeding season in wild, free-ranging deer and associations with antler size have not been reported. Levels of IGF-I during the breeding season could also effect reproductive success by influencing an individual's ability to build muscle mass (Douglas et al., 1991; Oddy and Owens, 1996). Male cervids increase muscle mass prior to the breeding season in preparation for intrasexual combat (Verme and Ullrey, 1984), an important component of the mate selection process in cervids. However, an association between systemic IGF-I levels and muscle mass in free-ranging male cervids has not been established to date.

Numerous studies have documented genotypic effects on systemic levels of IGF-I in domestic livestock (Echternkamp et al., 1990; Spicer et al., 1993; Simpson et al., 1994, 1997). If there is a genetic basis for systemic levels of IGF-I, and IGF-I indirectly influences reproductive success in male deer, then IGF-I should be investigated to determine its influence on life-history strategies and breeding success. Because little information is available regarding systemic levels of IGF-I in adult, male white-tailed deer (*Odocoileus virginianus*) from a free-ranging population, the present experiment was conducted to determine if: (1) systemic concentrations of IGF-I are associated with serum testosterone in adult, male white-tailed deer during the breeding season; (2) concentrations of serum IGF-I in adult, male white-tailed deer change during or following the breeding season; (3) levels of IGF-I are affected by age in male deer; and (4) levels of IGF-I during the breeding season are associated with select morphometric measures.

2. Materials and methods

Our study population consisted of white-tailed deer at the McAlester Army Ammunition Plant (McAAP) in southeastern Oklahoma. The McAAP herd had been managed using quality deer objectives since 1989 (Ditchkoff et al., 1996, 1997) and thus had a large proportion ($>50\%$; Ditchkoff et al., 2000) of mature males (≥ 3.5 years old) for sampling. Predominant vegetation types at McAAP are meadows of native prairie grass (*Andropogon virginicus*, *A. gerardii*, and *Schizachyrium scoparium*) bisected by brushy draws (*Ulmus alata*, *Symphoricarpos orbiculatus*, *Prunus angustifolia*, and *Diospyros virginiana*), oak (*Quercus nigra*, *Q. shumardii*) bottoms, and post oak (*Q. stellata*)–blackjack oak (*Q. marilandica*) uplands. The study area is further described by Ditchkoff et al. (1996, 1997).

We collected data from hunter harvested deer during 8 October–16 November 1994–1996 ($n = 263$) and deer captured using drop-nets during December–January 1994–1996 ($n = 80$). Most births of white-tailed deer at McAAP occur in late May or early June (Caire et al., 1989) indicat-

ing that most breeding takes place during early November (200-day gestation period; Armstrong, 1950). However, fawns may appear in early May (mid-October conception; W.R. Starry, McAAP Land Manager, personal communication) and thus we loosely define the breeding season as a period from early October to late November. Antlers were measured according to the Boone and Crockett scoring system described by Nesbitt and Wright (1981). Boone and Crockett score is a trophy scoring system where scores for each antler are summed together with the inside spread (greatest distance between the main beams) to obtain an overall estimate of antler development. This system measures length of each tine, length of the main beam, and circumferences around the main beam at the base of the antler (basal circumference) and between successive tines (not to exceed 4 circumferences for each antler). We did not measure length of all tines during 1994 so we could not calculate antler scores during that year. We measured chest girth, skull length, right hind-foot length, and body length to the nearest 0.1 cm on each animal. Field-dressed carcass mass was measured to the nearest 0.5 kg on those deer harvested by hunters. Deer were aged by tooth wear and eruption (Severinghaus, 1949).

We collected blood from the thoracic cavity of hunter-harvested deer and from captured deer via jugular venipuncture into 10-ml evacuated serum-separating tubes (SST; Becton Dickinson Vacutainer Systems, Rutherford, NJ, USA). Serum was separated by centrifugation within 6 h of collection and stored at −85°C. Concentrations of serum IGF-I were determined by acid-ethanol extraction (16 h at 4°C) radioimmunoassay previously described (Echternkamp et al., 1990; Suttie et al., 1991a,b) and validated for deer serum. We used recombinant human/bovine IGF-I as the standard which differs from cervine IGF-I by only two amino acids (Moore et al., 1993). The inter- and intra-assay CV were 4.7 and 5.2%, respectively.

Serum testosterone levels were assayed with a direct RIA procedure (Coat-A-Count Testosterone, Diagnostics Products Corporation, Los Angeles, CA, USA). Following the Coat-A-Count methodology, we added 50 μl of serum and 1.0 ml of ^{125}I testosterone to antibody-labeled tubes prior to incubation for 3 h at 37°C. Each Coat-A-Count tube was pre-labeled with monoclonal antibodies to testosterone. Following incubation, samples were thoroughly aspirated and radioactivity of tubes was counted in a gamma counter. Each sample was assayed in duplicate and samples with error $>5\%$ were reanalyzed. This assay is sensitive to testosterone concentrations ≥ 4 ng/dl, and interassay percentage CV is 5–12%.

We compared serum IGF-I and testosterone during the breeding season among age classes using analysis of covariance (ANCOVA) with date of sampling as a covariate to control for time effects. We originally tested for a year effect in all analyses, but because year was not significant ($P > 0.05$) we dropped it from the models. We tested for changes in IGF-I and testosterone concentrations during the breeding season by categorizing date of sampling into 1-week intervals and using an ANCOVA with week as a main effect and age as a covariate. We made multiple comparisons using least square means. We used multiple regression to determine if measures of body size were associated with IGF-I when controlling for age. We used analysis of variance with age and season as main effects to test for seasonal (breeding vs. post-breeding) differences in IGF-I and testosterone. When appropriate, multiple comparisons were made using Fisher's Least Squares Differences (LSD) Procedure (Hicks, 1993). We tested for associations between serum concentrations of IGF-I and testosterone during and following the breeding season using simple correlations. All analyses were performed using the Statistical Analysis System (SAS Institute Inc., 1990).

3. Results

During the breeding season, IGF-I concentrations ranged from 5.81 to 224.9 ng/ml with and overall mean concentration of 63.6 ng/ml ($n = 189$; S.E. = 2.5) with greatest concentrations tending to occur in deer from 2.5 to 5.5 years of age. During the breeding season, we found that young (1.5 years old) and old (≥ 6.5 years old) adult males had lower levels of IGF-I than males 2.5, 3.5 and 5.5 years old (Fig. 1). Least square means of IGF-I of 1.5-year-old ($P = 0.291$) and ≥ 6.5-year-old ($P = 0.331$) deer did not differ from 4.5-year-old deer. Serum IGF-I was less ($P = 0.001$) in deer following the breeding season ($n = 65$; mean = 34.6; S.E. = 2.0) than during the breeding season, and we found that 3.5- and 4.5-year-old

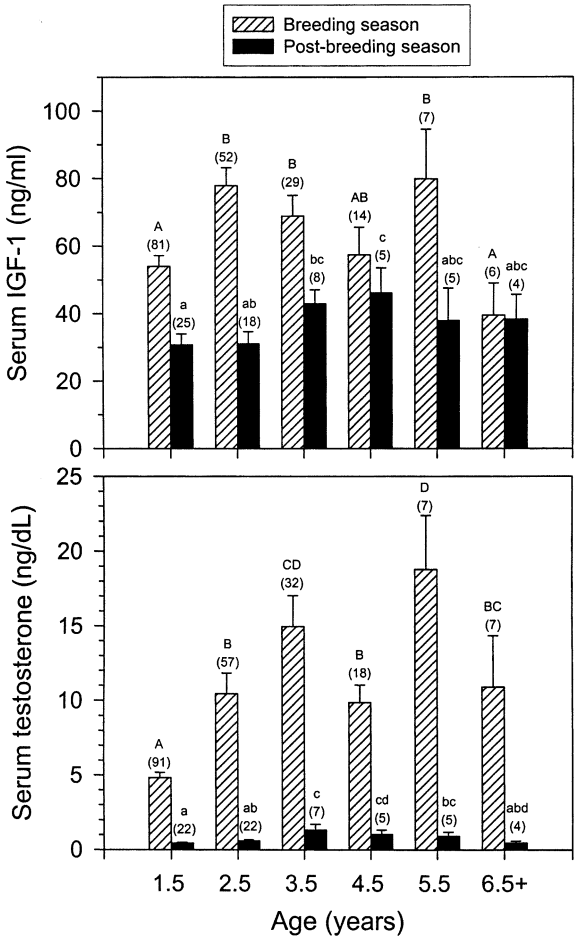

Fig. 1. Mean serum IGF-I and testosterone of different age classes of male white-tailed deer during and following the breeding season. Breeding season means without a common capital letter are different ($P < 0.05$), and post-breeding season means without a common lower case letter are different ($P < 0.05$). Numbers in parentheses are sample sizes.

deer had greater ($P < 0.05$) serum IGF-I than 1.5-year-old deer.

Serum IGF-I tended to decrease ($P = 0.001$) by approximately 40% during the breeding season (6 October–17 November) when controlling for age with ANCOVA (Fig. 2). Multiple regression models suggested that field-dressed body mass ($R^2 = 0.23$) and antler score ($R^2 = 0.12$) had a positive ($P < 0.05$) association with IGF-I concentration during the breeding season when including age in the model (Table 1). Chest girth, skull length, mean teste mass, and inside spread of antlers, while tending to be positively associated ($P < 0.05$) with IGF-I concentration in multiple regression analyses, had low (< 0.08) values of R^2. Body length and hind foot length were not related ($P > 0.117$) to IGF-I concentration during the breeding season.

Serum testosterone was correlated positively ($r = 0.39$; d.f. = 200; $P = 0.001$) with serum IGF-I during the breeding season (Fig. 3). This positive correlation was also found within 1.5- ($r = 0.26$; d.f. = 94; $P = 0.012$) and 2.5-year-old age classes ($r = 0.55$; d.f. = 51; $P = 0.001$), but not present among groups of deer that were 3.5 ($r = 0.13$; d.f. = 28; $P = 0.519$), 4.5 ($r = 0.39$; d.f. = 14; $P = 0.168$), or ≥ 5.5 years old ($r = 0.11$; d.f. = 13; $P = 0.719$). Serum testosterone was also correlated positively ($r = 0.28$; d.f. = 58; $P = 0.034$) with serum IGF-I following the breeding season, but we did not detect associations between testos-

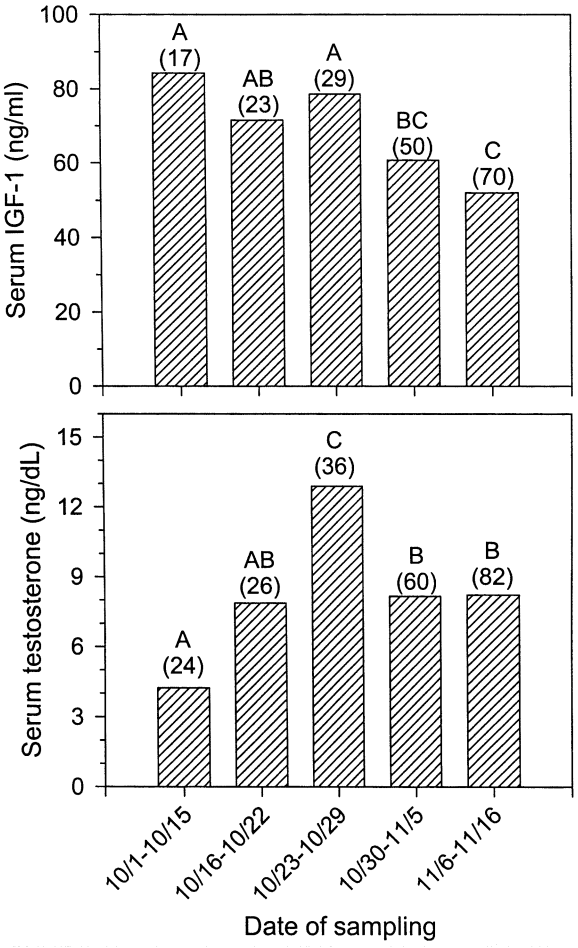

Fig. 2. Least square means of serum IGF-I and testosterone of male white-tailed deer during different weeks of the breeding season. Bars without a common letter are statistically different ($P < 0.05$) based upon an analysis of covariance with age as a covariate. Numbers in parentheses are sample sizes.

Table 1
Relationships between measures of body and antler size, and serum IGF-I concentrations of adult, male white-tailed deer during the breeding season using multiple regressions to control for age effects

Body size measure	Body or antler size			Age (years)			Intercept			
	Est.	S.E.	*P*	Est.	S.E.	*P*	Est.	S.E.	*P*	r^2
Body size measurements[a]										
Body mass	1.20	0.16	0.001	−12.8	2.4	0.001	−24.4	12.4	0.051	0.232
Chest girth	0.04	0.02	0.009	−0.6	1.8	0.741	26.7	14.2	0.061	0.038
Skull length	0.25	0.06	0.001	−1.8	1.8	0.326	−6.8	18.1	0.707	0.078
Body length	0.00	0.03	0.878	0.6	1.8	0.733	61.6	6.1	0.001	0.001
Hind foot length	0.01	0.04	0.728	0.6	1.7	0.713	56.6	15.9	0.001	0.002
Teste mass	0.62	0.30	0.044	−1.2	2.0	0.569	41.3	10.5	0.001	0.028
Antler size measurements[b]										
Antler score	0.52	0.12	0.001	−9.7	2.9	0.001	52.7	6.6	0.001	0.122
Inside spread	1.05	0.33	0.002	−5.0	2.5	0.044	47.9	7.3	0.001	0.058

[a] Units for body mass are kilograms; for teste mass are grams; and for all lengths are centimeters.
[b] Units for antler measurements are inches because the Nesbitt and Wright (1981) scoring system for antlers uses inches.

terone and IGF-I ($P > 0.05$) within age groups during this period. Serum testosterone was greatest ($P < 0.05$) among 3.5- and 5.5-year-old deer during the breeding season and lowest ($P < 0.05$) among 1.5-year-old deer (Fig. 1). Testosterone levels decreased ($P = 0.008$) up to 90% following the breeding season and tended to be lowest among deer that were 1.5 and ≥ 6.5 years old. During the breeding season, testosterone levels increased ($P < 0.05$) until the end of October and decreased during November (Fig. 2).

4. Discussion

Our data indicate that age influences circulating levels of IGF-I in adult, male white-tailed deer during the breeding season. Male deer that were 2.5–5.5 years old had greater levels of IGF-I than young (1.5 years old) and old (≥ 6.5 years old) adult males. While this trend has not been examined among cervids, these data corroborate evidence suggesting that IGF-I decreases in aged individuals among all animal species studied to date including humans (Zadik et al., 1985; Ghigo et al., 1996) and rats (Tanaka et al., 1996). While our data does not provide a physiological explanation for the observed decrease of IGF-I with age, it does suggest that senescence may begin as early as 6.5 years old in white-tailed deer. An earlier study on seasonal changes in reproductive hor-

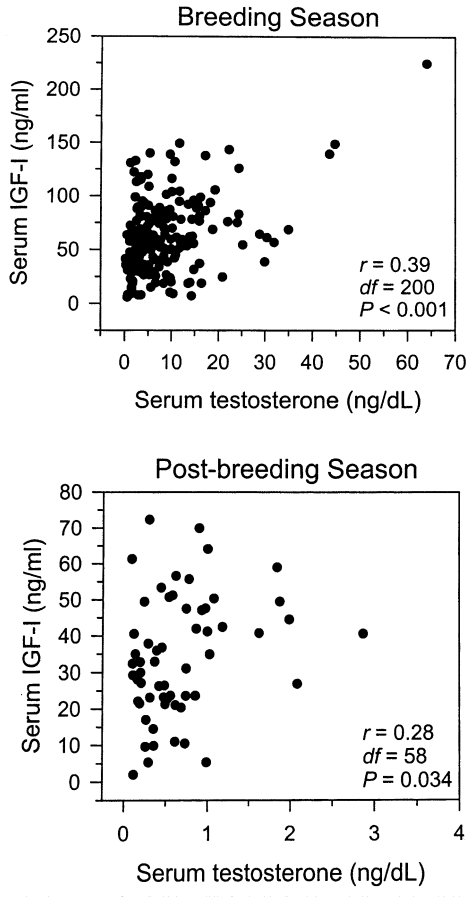

Fig. 3. Associations between serum IGF-I and testosterone in male white-tailed deer during and following the breeding season.

mones indicates that the prime age of male white-tailed deer from boreal populations is approximately 5–7 years (Bubenik and Schams, 1986), and a recent study of mortality in free-ranging ungulates has suggested that senescence does occur by 8 years (Loison et al., 1999).

Mean levels of IGF-I in our study decreased throughout the breeding season, possibly because of declining nutrition, changing photoperiod, and exhaustion from breeding activities. Nutrition has been found to significantly affect circulating levels of IGF-I in both free-ranging (Adam et al., 1995; Webster et al., 1996) and domestic ungulates (Richards et al., 1995; Bossis et al., 1999). As the breeding season progresses, adult, male white-tailed deer typically spend less time foraging and more time involved in breeding activities (Marchinton and Hirth, 1984). As a result, male deer can become chronically undernourished during the breeding season, often enough that rates of mortality in reproductively active males increase following the breeding season (Klein and Olson, 1960; Clutton-Brock et al., 1982; Ditchkoff, 2000). Indices of kidney and back fat in our deer decreased during the breeding season (S.S. Ditchkoff, unpublished data), suggesting that these animals tended to be in a negative state of energy balance. Levels of IGF-I also decreased after the breeding season, following expected patterns of nutrition as well. Although foraging time increases among male white-tailed deer following the breeding season (Marchinton and Hirth, 1984), nutritional value of potential forages is lowest during this season (winter; Waller et al., 1972). As a result, we would expect levels of IGF-I to be lowest during winter because of poor nutrition. Contrary to our data, Bubenik et al. (1998) found that IGF-I levels did not decrease in captive male reindeer following the breeding season, possibly because of supplemental feed. Photoperiod has also been shown to be associated positively with concentrations of IGF-I in male reindeer (*Rangifer tarandus*; Suttie et al., 1991b) and dairy cows (Dahl et al., 1997) and, therefore, may have also contributed to the decrease in IGF-I during and following the breeding season.

Body size and antler development were associated positively with concentration of IGF-I in serum during the breeding season. While not all measures of body size or antler development demonstrated this relationship, body mass and antler score, the best overall measures of body and antler development, both accounted for significant variation in IGF-I concentrations when controlling for age. Similar relationships were reported by Suttie et al. (1991a) who found strong positive associations between measures of body and antler size and concentrations of IGF-I in yearling red deer stags. Matthews et al. (1988) documented that transgenic mice expressing IGF-I had greater body mass than controls, suggesting that IGF-I probably does influence body size (Suttie et al., 1991a). Similarly, IGF-I has been directly associated with development of antlers in red deer (Suttie et al., 1989; Suttie and Fennessy, 1992), fallow deer (Bartoš et al., 2000), and roe deer (Schams et al., 1992), although this takes place prior to the breeding season when our data were collected.

Serum testosterone was associated positively with concentrations of IGF-I, suggesting that IGF-I may have some function in male white-tailed deer during the breeding season. Previous studies with red deer (Adam et al., 1995) have reported associations between production of testosterone and IGF-I secretion, and IGF-I has been shown to promote testosterone production by acting on Leydig cells (Lin et al., 1986; Lin, 1995; Le Roy et al., 1999). Mean levels of serum testosterone increased during the breeding season until late October, approximately 1–2 weeks before the peak of the rut. This is similar to patterns reported by Miller et al. (1987) and McMillin et al. (1974) for captive white-tailed deer, and Mirarchi et al. (1978) for captive and wild white-tailed deer. Testosterone tends to peak and then decline prior to the peak of the breeding season, which is important for promoting aggressive behavior in males and establishing dominance during intrasexual competition (Lincoln and Guinness, 1973; Monfort et al., 1993), ultimately acting to enhance reproductive success. If IGF-I does influence testosterone production in male deer, then the importance of IGF-I in the breeding male cervid cannot be understated due to the manner in which testosterone influences breeding success.

Although this is the first report for mean levels of IGF-I in serum of adult, male white-tailed deer, these values were within the range of previously published values for captive deer species (Suttie et al., 1989, 1991a; Suttie and Fennessy, 1992; Enright et al., 1994; Adam et al., 1995; Webster et al., 1996; Reyes et al., 1997; Bartoš et

al., 1998; Bubenik et al., 1998). In addition, our data provide patterns of IGF-I for free-ranging, adult, male white-tailed deer during the breeding season and document age, temporal, and morphometric relationships with levels of IGF-I. Because concentration of testosterone in the serum was associated positively with IGF-I, it is possible that IGF-I could play an indirect role in the breeding male cervid. While previous authors have hypothesized that IGF-I plays an important role in reproduction in other species (Lin, 1995; Lin et al., 1998), further work is needed to elucidate any potential role that IGF-I may have in reproduction of male deer.

Acknowledgements

We wish to thank E.R. Welch, Jr., D.E. Townsend II, and S.T. Grubbs for their help in collecting data. W.R. Starry, B.J. Farrar, and W.C. Dinkines provided support at our study area, and R.P. Wettemann and L. Mackey provided logistical support with testosterone assays. This project was funded by the United States Army and the National Science Foundation (BSR-8657043, IBN-9318066). We also thank the Oklahoma Cooperative Fish and Wildlife Research Unit (Oklahoma Department of Wildlife Conservation, Oklahoma State University, Wildlife Management Institute, and United States Geological Survey's Biological Resource Division, cooperating) for logistic support. This research was approved by the Oklahoma State University Institutional Animal Care and Use Committee as protocol number 461.

References

Adam, C.L., Kyle, C.E., Young, P., Atkinson, T., 1995. Effect of nutritional growth restriction on timing of reproductive development and plasma concentrations of insulin-like growth factor-1 and growth hormone in male red deer (*Cervus elaphus*) reared in constant photoperiod. J. Anim. Sci. 61, 155–160.

Armstrong, R.A., 1950. Fetal development of the northern white-tailed deer (*Odocoileus virginianus borealis* Miller). Am. Mid. Nat. 43, 650–666.

Bartoš, L., Reyes, E., Schams, D., Bubenik, G., Lobos, A., 1998. Rank dependent seasonal levels of IGF-1, cortisol and reproductive hormones in male pudu (*Pudu puda*). Comp. Biochem. Physiol. 120A, 373–378.

Bartoš, L., Schams, D., Kierdorf, U. et al., 2000. Cyproterone acetate reduced antler growth in surgically castrated fallow deer. J. Endocrinol. 164, 87–95.

Bossis, I., Wettemann, R.P., Welty, S.D., Vizcarra, J.A., Spicer, L.J., Diskin, M.G., 1999. Nutritionally induced anovulation in beef heifers: ovarian and endocrine function preceding cessation of ovulation. J. Anim. Sci. 77, 1536–1546.

Bubenik, G.A., Schams, D., 1986. Relationships of age to seasonal levels of LH, FSH, prolactin and testosterone in male, white-tailed deer. Comp. Biochem. Physiol. A 83, 179–183.

Bubenik, G.A., Schams, D., White, R.G., Rowell, J., Blake, J., Bartoš, L., 1998. Seasonal levels of metabolic hormones and substrates in male and female reindeer (*Rangifer tarandus*). Comp. Biochem. Physiol. 120C, 307–315.

Caire, W., Tyler, J.D., Glass, B.P., Mares, M.A., 1989. Mammals of Oklahoma. University of Oklahoma Press, Norman, OK.

Clutton-Brock, T.H., Guinness, F.E., Albon, S.D., 1982. Red deer: behavior and ecology of two sexes. University of Chicago Press, Chicago, IL.

Dahl, G.E., Elsasser, T.H., Capuco, A.V., Erdman, R.A., Peters, R.R., 1997. Effects of a low daily photoperiod on milk yield and circulating concentration of insulin-like growth factor-I. J. Dairy Sci. 80, 2784–2789.

Ditchkoff, S.S., 2000. Honest advertisement in male white-tailed deer: evidence for the handicap hypothesis of mate selection. Ph.D. Dissertation, Oklahoma State University, Stillwater, OK.

Ditchkoff, S.S., Welch Jr., E.R., Lochmiller, R.L., Masters, R.E., Dinkines, W.C., Starry, W.R., 1996. Deer harvest characteristics during compound and traditional archery hunts. Proc. Annu. Conf. Southeast. Assoc. Fish Wildl. Agenc. 50, 391–396.

Ditchkoff, S.S., Welch Jr., E.R., Starry, W.R., Dinkines, W.C., Masters, R.E., Lochmiller, R.L., 1997. Quality deer management at the McAlester Army Ammunition Plant: a unique approach. Proc. Annu. Conf. Southeast. Assoc. Fish Wildl. Agenc. 51, 389–399.

Ditchkoff, S.S., Welch Jr., E.R., Lochmiller, R.L., 2000. Using cast antler characteristics to profile quality of white-tailed deer *Odocoileus virginianus* populations. Wildl. Biol. 6, 23–28.

Douglas, R.G., Gluckman, P.D., Ball, K., Breier, B., Shaw, J.H., 1991. The effects of infusion of insulin-like growth factor (IGF)-I, IGF-II, and insulin on glucose and protein metabolism in fasted lambs. J. Clin. Invest. 88, 612–622.

Echternkamp, S.E., Spicer, L.J., Gregory, K.E., Canning, S.F., Hammond, J.M., 1990. Concentrations of insulin-like growth factor-I in blood and ovarian follicular fluid of cattle selected for twins. Biol. Reprod. 43, 8–14.

Enright, W.J., Spicer, L.J., Culleton, N., Kelly, M., Prendiville, D.J., 1994. Effect of nutrition on body weight, puberty, and plasma concentration of progesterone and insulin-like growth factor-I in fallow deer. Irish J. Agric. Food Res. 33, 88 (abstract).

Froesch, E.R., Schmid, C., Schmander, J., Zapf, J., 1985. Actions of insulin-like growth factors. Ann. Rev. Physiol. 47, 443–467.

Ghigo, E., Arvat, E., Goffi, S. et al., 1996. Human aging and the GH-IGF-I axis. J. Pediat. Endocrinol. Metab. 9, 271–278.

Hicks, C.R., 1993. Fundamental Concepts in the Design of Experiments, 4th ed Saunders Publishing, New York.

Horikawa, R., Asakawa, K., Hizuka, N., Takano, K., Shizume, K., 1989. Growth hormone and insulin-like growth factor I stimulate Leydig cell steroidogenesis. Eur. J. Pharmacol. 166, 87–94.

Jones, J.I., Clemmons, D.R., 1995. Insulin-like growth factors and their binding proteins: biological actions. Endocrinol. Rev. 16, 3–34.

Klein, D.R., Olson, S.T., 1960. Natural mortality patterns of deer in southeast Alaska. J. Wildl. Manage. 24, 80–88.

Le Roy, C., Lejeune, H., Chuzel, F., Saez, J.M., Langlois, D., 1999. Autocrine regulation of Leydig cell differentiated functions by insulin-like growth factor I and transforming growth factor beta. J. Steroid Biochem. Mol. Biol. 69, 379–384.

Lin, T., 1995. Regulation of Leydig cell function by insulin-like growth factor-I and binding proteins. J. Androl. 16, 193–196.

Lin, T., Haskell, J., Vinson, N., Terracio, L., 1986. Direct stimulatory effects of insulin-like growth factor-I on Leydig cell steroidogenesis in primary culture. Biochem. Biophys. Res. Commun. 137, 950–956.

Lin, T., Wang, D., Hu, J., Stocco, D.M., 1998. Upregulation of human chorionic gonadotrophin-induced stereogenic acute regulatory protein by insulin-like growth factor-I in rat Leydig cells. Endocrine 8, 73–78.

Lincoln, G.A., Guinness, F., 1973. The sexual significance of the rut in red deer. J. Reprod. Fert. Suppl. 19, 475–489.

Loison, A., Festa-Bianchet, M., Gaillard, J.-M., Jorgensen, J.T., Jullien, J.-M., 1999. Age-specific survival in five populations of ungulates: evidence of senescence. Ecology 80, 2539–2554.

Matthews, L.S., Hammer, R.E., Behringer, R.R. et al., 1988. Growth enhancement of transgenic mice expressing human insulin-like growth factor 1. Endocrinology 123, 2827–2833.

Marchinton, R.L., Hirth, D.H., 1984. Behavior. In: Halls, L.K. (Ed.), White-Tailed Deer: Ecology and Management. Stackpole Books, Harrisburg, PA, pp. 129–168.

McMillin, J.M., Seal, U.S., Kennlyne, K.D., Erickson, A.W., Jones, J.E., 1974. Annual testosterone rhythms in the adult white-tailed deer (*Odocoileus virginianus borealis*). Endocrinology 94, 1034–1040.

Miller, K.V., Marchinton, R.L., Forand, K.J., Johansen, K.L., 1987. Dominance, testosterone levels, and scraping activity in a captive herd of white-tailed deer. J. Mamm. 68, 812–817.

Mirarchi, R.E., Howland, B.E., Scanlon, P.F., Kirkpatrick, R.L., Samford, L.M., 1978. Seasonal variation in plasma LH, FSH, prolactin, and testosterone concentrations in adult male white-tailed deer. Can. J. Zool. 56, 121–127.

Monfort, S.L., Brown, J.L., Bush, M. et al., 1993. Circannual inter-relationships among reproductive hormones, gross morphometry, behaviour, ejaculate characteristics and testicular histology in Eld's deer stags (*Cervus eldi thamin*). J. Reprod. Fert. 98, 471–480.

Moore, L.G., Jones, D., Lymburn, M.A. et al., 1993. Isolation and sequencing of deer and sheep insulin-like growth factors-I and -II. Gen. Comp. Endocrinol. 92, 302–310.

Nesbitt, W.H., Wright, P.L., 1981. Records of North American big game. Boone and Crockett Club, Alexandria, VA.

Oddy, V.H., Owens, P.C., 1996. Insulin-like growth factor I inhibits degradation and improves retention of protein in hindlimb muscle of lambs. Am. J. Physiol. 271, E973–982.

Rechler, M.M., Nissley, S.P., 1985. The nature and regulation of the receptors of insulin-like growth factors. Ann. Rev. Physiol. 47, 425–442.

Reyes, E., Bubenik, G.A., Lobos, A., Schams, D., Bartoš, L., 1997. Seasonal levels of cortisol, IGF-1 and triiodothyronine in adult male pudu (*Pudu puda*). Folia Zool. 46, 109–116.

Richards, M.W., Spicer, L.J., Wetteman, R.P., 1995. Influence of diet and ambient temperature on bovine serum insulin-like growth factor-I and thyroxine: relationships with non-esterified fatty acids, glucose, insulin, luteinizing hormone and progesterone. Anim. Reprod. Sci. 37, 267–279.

SAS Institute Inc., 1990. SAS/STAT user's guide. SAS Institute Inc., Cary, NC.

Severinghaus, C.W., 1949. Tooth development and wear as criteria for age in white-tailed deer. J. Wildl. Manage. 13, 195–216.

Schams, D., Barth, D., Heinze-Mutz, E.-M., Pflaum, G., Karg, H., 1992. Antler growth in roe deer: effects of casting and correlations with growth hormone and insulin like growth factor I. In: Brown, R.D. (Ed.), The Biology of Deer. Springer-Verlag, New York, NY, pp. 505–510.

Simpson, R.B., Chase Jr., C.C., Spicer, L.J., Vernon, R.K., Hammond, A.C., Rae, D.O., 1994. Effects of

exogenous insulin on plasma and follicular insulin-like growth factor I, insulin-like growth factor binding protein, follicular oestradiol and progesterone, and follicular growth in superovulated Angus and Brahman cows. J. Reprod. Fert. 102, 483–492.

Simpson, R.B., Chase Jr., C.C., Spicer, L.J., Carroll, J.A., Hammond, A.C., Welsh Jr., T.H., 1997. Effect of exogenous estradiol on plasma concentrations of somatotropin, insulin-like growth factor-I, insulin-like growth factor binding protein activity, and metabolites in ovariectomized Angus and Brahman cows. Dom. Anim. Endocrinol. 14, 367–380.

Spicer, L.J., Tinker, E.D., Wettemann, R.P., Buchanan, D.S., 1993. Relationship between genotype of sire and dam, and plasma insulin-like growth factor-I concentrations in crossbred cows post partum. Livestock Prod. Sci. 33, 355–360.

Spicer, L.J., Echternkamp, S.E., 1995. The ovarian insulin and insulin-like growth factor system with an emphasis on domestic animals. Dom. Anim. Endocrinol. 12, 223–245.

Suttie, J.M., Fennessy, P.F., 1992. Recent advances in the physiological control of velvet antler growth. In: Brown, R.D. (Ed.), The Biology of Deer. Springer-Verlag, New York, NY, pp. 471–486.

Suttie, J.M., Fennessy, P.F., Corson, I.D. et al., 1989. Pulsatile growth hormone, insulin-like growth factors and antler development in red deer (*Cervus elaphus scoticus*) stags. J. Endocrinol. 121, 351–360.

Suttie, J.M., Corson, I.D., Gluckman, P.D., Fennessy, P.F., 1991a. Insulin-like growth factor 1, growth and body composition in red deer stags. Anim. Prod. 53, 237–242.

Suttie, J.M., White, R.G., Breier, B.H., Gluckman, P.D., 1991b. Photoperiod associated changes in insulin-like growth factor-I in reindeer. Endocrinology 129, 679–682.

Tanaka, H., Barnes, J., Liang, C.T., 1996. Effects of age on the expression of insulin-like growth factor-I, interleukin-6, and transforming growth factor-β mRNAs in rat femurs following marrow ablation. Bone 18, 473–478.

Verme, L.J., Ullrey, D.E., 1984. Physiology and nutrition. In: Halls, L.K. (Ed.), White-Tailed Deer: Ecology and Management. Stackpole Books, Harrisburg, PA, pp. 91–118.

Waller, G.R., Morrison, R.D., Nelson, A.B., 1972. Chemical composition of native grasses in central Oklahoma from 1947–1962. Oklahoma Agricultural Experiment Station Bulletin B-697.

Webster, J.R., Corson, I.D., Littlejohn, R.P., Stewart, S.K., Suttie, J.M., 1996. Effects of season and nutrition on growth hormone and insulin-like growth factor-I in male red deer. Endocrinology 137, 698–704.

Zadik, Z., Chalew, S.A., McCarter, R.J., Meistas, M., Kowarski, A.A., 1985. The influence of age on the 24-hour integrated concentration of growth hormone in normal individuals. J. Clin. Endocrinol. Metab. 60, 513–516.