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Research Article

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Insulin-like Growth Factor 1 and Prolactin Levels in Chimpanzees (Pan troglodytes) Across the Lifespan

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Abstract

As human and chimpanzee genomes show high homology for *IGF1* and *PRL*, we analyzed the sera of 367 healthy chimpanzees obtained during routine physical examinations in a single colony and measured chimpanzee insulin-like growth factor (IGF)-1 and prolactin (PRL) levels across the lifespan using standard human immunoassays. Assuming chimpanzee IGF-1 levels peak during puberty as in humans, we randomly defined puberty as the age at which most IGF-1 levels were equal to or above the 90th percentile for each sex (males, ages ≥7.00 but <9.20 years; females, ≥5.00 but <8.00 years). IGF-1 levels steadily increased at a similar rate in juvenile males and females and peaked in puberty, strongly correlating with age, then slowly decreased faster in adult males than in adult females. As a group, males had a higher mean IGF-1 level than did females, but comparison by age category showed similar mean IGF-1 levels in males and females. PRL levels increased with age in females more than in males and levels were twice as high in females than in males. One pubertal male reported to have short stature had lower IGF-1 and weight compared with other males in the age group, confirming suspected growth hormone deficiency; a second male of normal height but low IGF-1 may have had delayed puberty. Overall, results show that differences in IGF-1 levels over the lifespan in this cohort of chimpanzees largely mimic those seen in humans, while patterns of PRL changes are less similar.

Key Words: Pan troglodytes, chimpanzee, insulin-like growth factor 1, prolactin

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Introduction

Sequencing human and chimpanzee (Pan troglodytes) genomes shows that protein-coding genes are highly homologous [1], and *IGF1* and *PRL* gene coding sequences show >99.3% homology between the 2 species [2, 3]. Immunoassays designed to measure human hormones have been successfully used in chimpanzees to measure prolactin (PRL) in serum [4–6] as well as insulin-like growth factor (IGF) binding protein 3 (IGFBP3) in urine [7] to assess changes in hormones at different stages of life. However, available data are primarily derived from small samples of chimpanzees in tight age brackets and/or in only one sex [4–6, 8–11]. To our knowledge, there is no defined set of normal values for IGF-1 or PRL across the lifespan in any large cohort of male and female chimpanzees.

Clinical features of growth hormone (GH) deficiency are rarely observed in chimpanzees and, to our knowledge, there are no published reports describing GH deficiency in this species. We used commercially available human immunoassays to assess IGF-1 and PRL levels in sera obtained from a large group of healthy chimpanzees living in a single colony and housed at a single facility. Our goal was to provide a range of normal values for this population to be used by veterinarians to better assess short-for-their age chimpanzees suspected of having GH deficiency.

Materials and Methods

Serum samples and body anthropomorphic measurements were obtained during routine physical examinations from chimpanzees housed at the New Iberia Research Center at the University of Louisiana at Lafayette in New Iberia, Louisiana. The collection of samples during physical examination is covered by an animal procedure statement approved by the University of Louisiana at Lafayette Institutional Animal Care and Use Committee (IACUC) and renewed and reviewed annually. The New Iberia Research Center and all of its programs are reviewed and approved under this committee on a semiannual basis.

Examinations were conducted throughout the year, but mostly during March/April and September/October. Chimpanzees were sedated between 7:00 and 11:00 AM with telazol (4–6 mg/kg IM) and ketamine HCL (10 mg/kg IM) to ensure immobilization for the physical examination and phlebotomy.

All animals spent time indoors and outdoors in same-sex groups. Some young animals spent up to 1 year in the nursery before being transferred as peer groups into indoor/outdoor caging. All animals were assumed to be fertile and all males of reproductive age underwent a vasectomy and were separated from the females. Females were not receiving hormone modulation for birth control and were not pregnant. All chimpanzees were known to be healthy at the time of physical examination and serum collection.

After standard blood testing was completed, residual aliquots of serum were frozen and shipped to Cedars-Sinai Medical Center, where they were stored at -80°C until batch processing. Samples were analyzed using commercially available immunoassays for assessment of human IGF-1 (Quantikine ELISA Human IGF-1 Immunoassay DG100; R&D Systems, Minneapolis, MN, USA) and human PRL (ADVIA Centaur Prolactin, Siemens Healthcare Diagnostics, Tarrytown, NY, USA). Assays were performed according to the manufacturer's instructions.

We assumed that chimpanzee IGF-1 levels peak during puberty as in humans, but we did not have information on their sexual development, such as Tanner staging for humans. Thus, rather than use the age categories previously defined to study thyroid function in this chimpanzee cohort [12], we calculated the age at which most IGF-1 levels were equal to or above the 90th percentile for each sex to determine puberty, and we determined age categories accordingly. Age was calculated in years, with additional months represented by a fraction of the year rounded to 2 digits. Based on mean IGF-1 levels for all male and female chimpanzees, age categories were defined in this study as: juvenile 0 to ≤7.00 years in males and 0 to ≤5.00 in females; puberty >7.00 but ≤9.20 years in males and >5.00 but ≤8.00 years in females; and adult >9.20 but ≤35.00 years in males and >8.00 but ≤35.00 years in females. Chimpanzees aged >35.00 years show a sharp increase in mortality [13] and are defined as elderly.

Categorical variables were summarized by frequency and percentage. For numerical variables, raw data are provided as mean ± standard deviation (SD) and are graphically summarized by mean ± standard error of the mean (SEM). Comparisons across 2 groups were assessed by the independent samples *t*-test. Analysis of variance (ANOVA) models with Tukey post hoc comparisons were used to assess numerical variables across more than 2 independent groups. Correlations between numerical variables were assessed by linear regression models. Regression models were used to ascertain differences in slopes between sexes by including an appropriate interaction term. A 2-sided 0.05 significance level was used throughout. Statistical calculations and graphs were made using Prism v5.04 (GraphPad Software, San Diego, CA, USA) and SAS v9.4 (SAS Institute, Cary, NC, USA).

Results

The study cohort comprised 367 chimpanzees, including 175 males (47.7%) and 192 females (52.3%).

When classified by age category, 15.5% were juveniles (23 male, 34 female), 10.6% were pubertal (23 male, 16 female), 67.3% were adults (120 male, 127 female), and 6.5% were elderly (9 male,15 female). Male and female weight distribution is presented in Fig. 1A and 1B, respectively. Combining all ages in each sex, males were heavier than females (Fig. 1C, $P < 0.0001$). A linear increase in weight was observed up to age 14.00 years in males (n = 71, slope 5.7 ± 0.3; r 0.92, $P < 0.0001$) and up to age 16.00 years in females (n = 93, slope 3.7 ± 0.1; r 0.94, $P < 0.0001$), with a higher increase rate in males ($P < 0.0001$) (Fig. 1D). Weight did not correlate with age after age 14.00 years in males and age 16.00 years in females.

IGF-1 levels

Mean IGF-1 levels per age year for all male and female chimpanzees are shown in Table 1. Two chimpanzees had IGF-1 levels well below that of their age category peers (Fig. 2A). One of the males, A6A001, was reported to have had short stature, sparse hair, and seborrhea, suggestive of GH deficiency. His parents and siblings were all reported to be healthy. He later developed mini-strokes and died at age 7.10 years; postmortem examination revealed midbrain congenital malformation. This male, along with A5A008, who also had very low IGF-1 but no clinical signs of GH deficiency, were excluded from group IGF-1 analyses and analyzed separately (discussed below).

Excluding the 2 chimpanzees with very low IGF-1 levels, in males, IGF-1 levels steadily increased in juveniles age 0 to ≤7.00 (62.9 ± 6.2 ng/mL per year), reaching the peak 90th percentile of 421.7 ng/mL during puberty (ages >7.00 and ≤9.20 years; Fig. 2A). In females, IGF-1 levels increased in juveniles age 0 to ≤5.00 (68.9 ± 5.6 ng/mL per year), reaching the peak 90th percentile of 393.9 ng/mL in puberty >5.00 and ≤8.00 years (Fig. 2B). Up to the end of this period, IGF-1 levels strongly correlate with age in males (r 0.84, $P < 0.0001$, Fig. 2C) and females (r 0.87, $P < 0.0001$, Fig. 2D), and increased at a similar rate in males and females ($P = 0.5$). During adulthood, IGF-1 levels slowly decreased in both males and females. In males ages >9.20 and ≤35.00 years, IGF-1 levels decreased at a rate of 8.4 ± 0.9 ng/mL per year and showed moderately negative correlation with age (r -0.64, $P < 0.0001$, Fig. 2E). In adult females ages >8.00 and ≤35.00 years, IGF-1 levels decreased more slowly than in males ($P < 0.0001$), at a rate of 2.6 ± 0.9 ng/mL per year and showed weakly negative correlation with age (r -0.25, $P = 0.005$, Fig. 2F).

Only 9 males and 17 females in the elderly category (age >35.00 years) were studied. These small numbers spanned large age periods (males, 36.00–51.00 years; females, 36.00–54.00 years), precluding meaningful correlation analyses.

Combining all ages, males had a higher mean IGF-1 level than did females (288.2 ± 9.1 vs 259.2 ± 7.5 ng/mL; t-test, $P = 0.01$, Fig. 3A). However, comparison across age categories shows similar mean IGF-1 levels in males and females (data not shown). As expected, pubertal males age >7.00 but ≤9.20 years

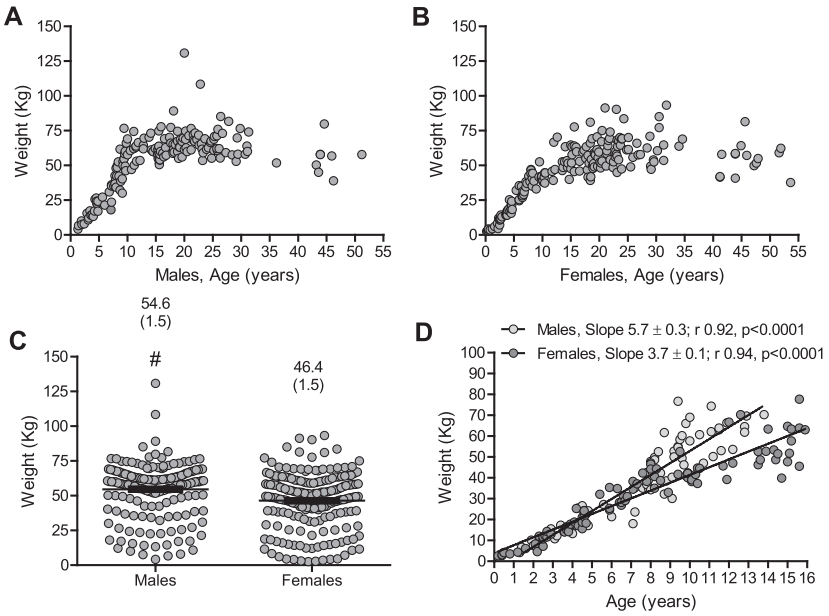

Figure 1. Chimpanzee weight (kg) by age. **(A)** Males (n = 175); **(B)** females (n = 192). **(C)** Weight at all ages in males (n = 175) vs females (n = 192). Mean (SEM) shown above each group; *t*-test, $^{\#}P < 0.0001$. **(D)** Regression line (slope) and correlation (r) of weight with age in males <14.00 years old (n = 71) vs females <16.00 years old (n = 93). Abbreviation: SEM, standard error of the mean.

Table 1. Serum IGF-1 levels (ng/mL) in male and female chimpanzees, by age (years)

	Males (n = 175)			Females (n = 192)		
Age (years)[a]	n	Mean	SD	n	Mean	SD
1.00	0	–	–	6	78.1	54.1
2.00	3	104.8	85.7	2	61.8	5.4
3.00	3	104.9	84.2	10	143.5	108.6
4.00	6	149.3	54.0	7	185.1	53.3
5.00	8	317.7	57.9	9	329.6	97.5
6.00	1	421.7	–	4	405.2	28.2
7.00	2	269.3	66.4	7	477.3	101.6
8.00[b]	12	462.9	166.8	5	489.5	46.7
9.00	8	487.9	140.6	8	348.2	54.2
10.00	12	418.0	96.9	6	293.0	75.1
11.00	4	357.9	64.5	6	246.2	67.5
12.00	7	338.8	45.3	2	229.0	37.0
13.00	4	327.6	85.7	3	254.7	64.4
14.00	1	319.6	–	4	241.8	31.4
15.00	5	347.2	65.6	5	247.9	47.1
16.00	16	284.9	32.2	9	282.7	75.0
17.00	5	251.8	50.5	3	340.8	35.3
18.00	5	219.5	58.6	5	245.8	97.8
19.00	8	254.8	50.9	11	217.1	66.5
20.00	6	267.8	59.0	10	253.6	45.7
21.00	7	261.9	86.1	6	220.2	81.4
22.00	7	258.4	77.2	9	275.6	59.4
23.00	5	272.8	70.1	4	242.9	54.5
24.00	5	231.6	34.0	12	256.3	29.9
25.00	4	204.0	33.8	3	223.5	84.2
26.00	7	188.9	36.5	4	255.0	19.1
27.00	4	210.8	67.0	2	190.5	63.2
28.00	2	147.7	95.4	1	254.1	–
29.00	1	229.2	–	2	191.4	104.5
30.00	4	211.7	100.3	4	193.6	27.5
31.00–40.00	5	217.6	47.6	8	275.2	44.4
41.00–50.00	7	210.4	63.7	12	218.8	50.6
51.00– 54.00	1	166.4	–	3	246.8	71.1

Abbreviations: IGF-1, insulin-like growth factor 1; SD, standard deviation.

[a]Includes chimpanzees from the end of the previous year up to and including the indicated age.

[b]Two male chimpanzees at this age had very low IGF-1 levels (IGF-1 69.4 and 73.0 ng/mL) and were analyzed separately. When excluded, mean ± SD IGF-1 levels at age 8.00 years is 494.4 ± 119.3.

and pubertal females age >5.00 but ≤8.00 years had higher mean IGF-1 levels compared with other age categories, as shown by a significant one-way ANOVA with $P < 0.0001$ with Tukey post hoc comparisons (Fig. 3B and 3C). The same analysis showed that adult females have higher IGF-1 levels than juvenile females (Fig. 3C). Mean IGF-1 in juvenile males ages 0 to ≤7.00 was 218.6 ± 24.5 ng/mL and 185.0 ± 21.5 ng/mL in juvenile females ages 0 to ≤5.00; 500.2 ± 25.6 ng/mL in pubertal males ages >7.00 to ≤9.20 and 463.1 ± 19.5 ng/mL in pubertal females ages >5.00 to ≤8.00; 270.6 ± 7.1 ng/mL in adult males age >9.20 to ≤35.00 and 257.5 ± 5.8 ng/mL in adult females age >8.00 to ≤35.00; and 206.5 ± 20.5 ng/mL in elderly males and 224.4 ± 13.8 ng/mL in elderly females, all >35.00 years old.

PRL levels

Mean PRL levels for all male and female chimpanzees are shown in Table 2. Four female chimpanzees showed PRL measurements above >202 ng/mL, which is the upper limit of the standard curve, and were excluded from analysis as outliers. PRL levels increased with age and correlated with age in males (r 0.27, $P = 0.0003$) and in females (r 0.4, $P < 0.0001$). PRL increase with age was significantly slower in males (0.35 ± 0.09 ng/mL per year) than in females (1.35 ± 0.2 ng/mL per year; $P = 0.0001$; Fig. 4A and 4B). Across all ages, mean PRL levels were twice as high in females (45.2 ± 2.8) than in males (22.7 ± 1.0; $P < 0.0001$) (Fig. 4C).

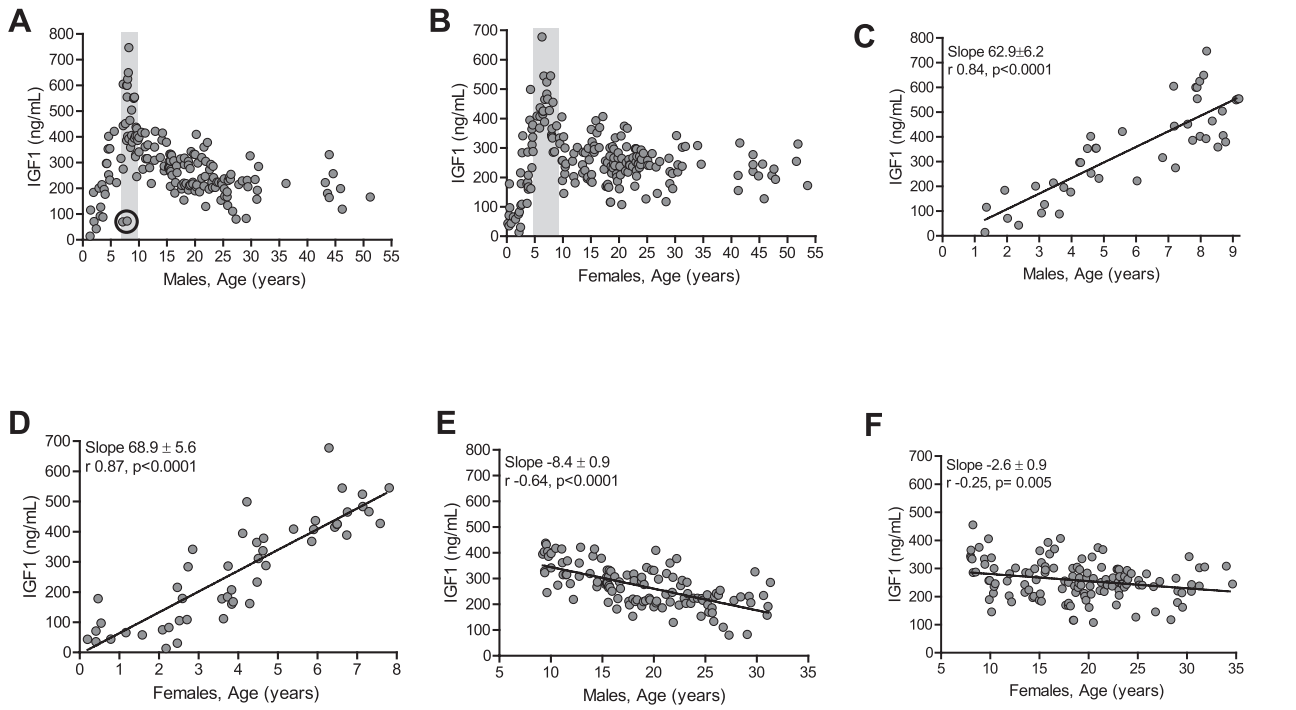

Figure 2. IGF-1 levels in male and female chimpanzees. **(A)** IGF-1 levels in males by age (n = 175). After removal of the 2 outliers (circled), gray vertical bar spans ages 7.00 to 9.20 years, during which most (67%) IGF-1 levels are equal to or above the 90th percentile of 421.7 ng/mL. **(B)** IGF-1 levels in females by age (n = 192). Gray vertical bar spans ages 5.00 to 8.00 years, during which most (88%) IGF-1 levels are equal to or above the 90th percentile of 393.9 ng/mL. **(C–F)** Regression line (slope) and correlation (r) of IGF-1 levels with age in **(C)** male juveniles and pubertal age ≤9.20 (n = 44); **(D)** female juveniles and pubertal age ≤8.00 years (n = 50); **(E)** male adults age >9.20 to ≤35.00 years (n = 120); and **(F)** female adults age >8.00 to ≤35.00 years (n = 127). Abbreviation: IGF-1, insulin-like growth factor 1.

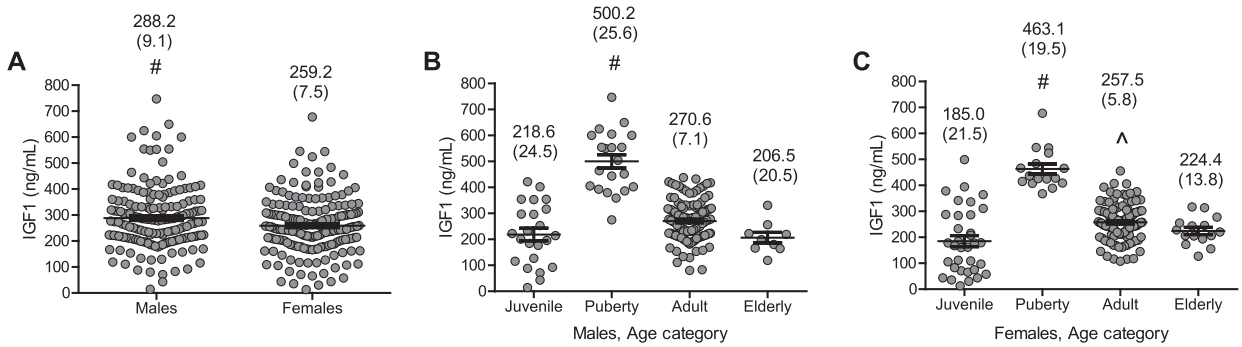

Figure 3. Comparisons of IGF-1 levels between male and female chimpanzees in different age categories. Mean (SEM) shown above each category. **(A)** IGF-1 levels at all ages in males (n = 173) vs females (n = 192). *t*-test, $^{\#}P < 0.0001$. **(B)** IGF-1 levels in males by age category. Juvenile, 0 to ≤7.00 years (n = 23); pubertal, >7.00 to ≤9.20 years (n = 20); adult, >9.20 years to ≤35.00 years (n = 119); elderly, >35.00 years (n = 9). One-way ANOVA with Tukey post hoc comparisons, $^{\#}P < 0.0001$ vs all other age categories. **(C)** IGF-1 levels in females by age category. Juvenile, 0 to ≤5.00 years (n = 34); pubertal, >5.00 to ≤8.00 years (n = 16); adult, >8.00 years to ≤35.00 years (n = 127); elderly, >35.00 years (n = 15). One-way ANOVA with Tukey post hoc comparisons, $^{\#}P < 0.0001$ vs all other age categories, $^{\wedge}P < 0.0001$ vs juveniles. Abbreviations: ANOVA, analysis of variance; IGF-1, insulin-like growth factor; SEM, standard error of the mean.

Male chimpanzees with low IGF-1

As noted above, two pubertal males, A6A001 and A5A008, had IGF-1 levels lower than other males in the same age category (n = 21), with mean IGF-1 levels of 71.2 ± 1.8 and 500.2 ± 25.6, respectively (*t*-test, $P < 0.0001$; Fig. 5A). PRL levels were similar (Fig. 5B).

A6A001 had a short stature suggestive of GH deficiency, sparse hair, and seborrhea. His weight was significantly less than the mean of male pubertal chimpanzees with normal IGF-1 levels (18 kg vs 40.2 ± 2.0 kg.) He had 7 siblings in the colony, 6 from the same sire only and 1 from the same sire and dam; all were healthy adults, as were his parents.

Table 2. Serum PRL levels (ng/mL) in male and female chimpanzees, by age (years)

	Males n = 175			Females N = 188		
Age (years)[a]	n	Mean	SD	n	Mean	SD
1.00	0	–	–	6	7.7	2.9
2.00	3	10.8	2.9	2	7.8	2.2
3.00	3	10.9	5.0	10	8.0	2.8
4.00	6	12.6	5.5	7	18.3	18.0
5.00	8	16.9	8.4	9	22.5	8.7
6.00	1	9.3	–	4	22.6	6.2
7.00	2	21.9	12.0	7	16.2	8.5
8.00	12	17.0	9.1	5	38.8	18.8
9.00	8	15.1	6.2	8	36.3	24.1
10.00	12	23.2	18.8	6	33.2	16.4
11.00	4	26.6	15.0	6	51.1	21.8
12.00	7	14.1	3.3	2	34.5	4.6
13.00	4	17.0	6.2	3	28.8	26.3
14.00	1	7.2	–	4	67.7	36.7
15.00	5	16.3	6.6	5	35.4	17.6
16.00	16	25.8	10.7	9	31.3	16.4
17.00[b]	5	27.5	10.7	2	34.4	15.4
18.00	5	25.3	15.6	5	55.6	37.9
19.00	8	32.1	8.4	11	60.7	31.1
20.00	6	29.0	11.1	10	45.3	41.8
21.00[b]	7	27.6	5.8	5	60.0	28.3
22.00	7	25.7	11.1	9	53.0	14.7
23.00	5	33.0	24.2	4	62.5	14.8
24.00	5	30.0	12.9	12	60.1	55.8
25.00	4	25.3	17.5	3	54.8	19.0
26.00[b]	7	26.7	12.9	3	54.7	32.3
27.00	4	34.8	21.5	2	64.3	61.0
28.00	2	20.1	2.7	1	47.9	–
29.00	1	17.9	–	2	104.1	77.3
30.00	4	11.0	5.4	4	48.2	18.8
31.00–40.00	5	25.0	13.9	8	47.3	14.1
41.00–50.00[b]	7	26.9	11.4	11	62.9	26.8
51.00–54.00	1	30.1	–	3	44.6	6.8

Abbreviations: PRL, prolactin; SD, standard deviation.

[a]Includes chimpanzees from the end of the previous year up to and including the indicated age.

[b]One female at this age had a PRL level >202 ng/mL, which is the upper limit of the standard curve, and was excluded as an outlier.

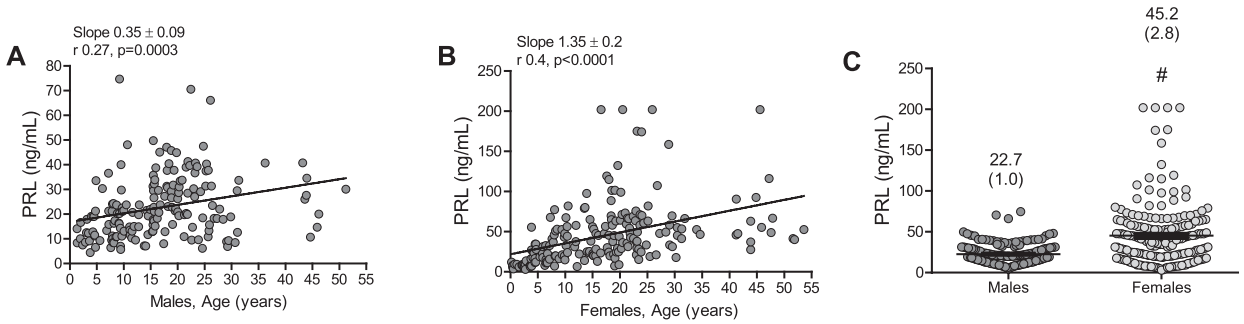

Figure 4. Comparisons of PRL levels between male (n = 175) and female (n = 192) chimpanzees across the lifespan. **(A–B)** Regression line (slope) and correlation (r) of PRL with age in males **(A)** and females **(B)**. Values above the standard curve (n = 4) were excluded. **(C)** PRL levels at all ages in males vs females. Mean (SEM) shown above each group; *t*-test, $^{\#}P < 0.0001$. Abbreviations: PRL, prolactin; SEM, standard error of the mean.

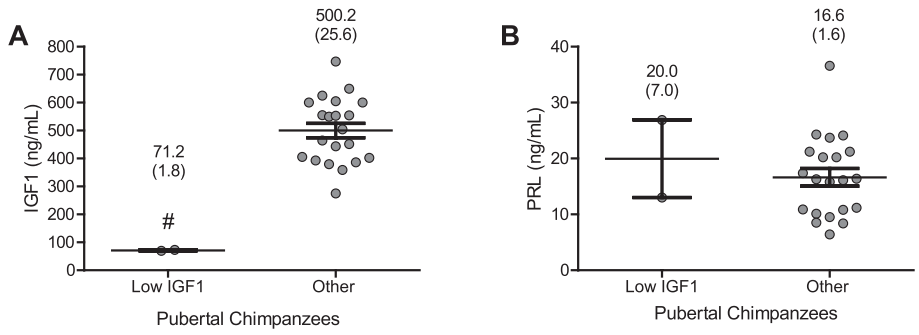

Figure 5. Comparisons between chimpanzees with low IGF-1 (n = 2) and all other chimpanzees in the same age category (n = 21) (pubertal, age >7.00 to ≤9.20 years). Mean (SEM) shown above each group. **(A)** IGF-1 levels; *t*-test, $^{\#}P < 0.0001$. **(B)** PRL levels. Abbreviations: IGF-1, insulin-like growth factor 1; PRL, prolactin; SEM, standard error of the mean.

A5A008, unrelated to A6A001, had no clinical signs suggestive of GH deficiency. Height was normal compared with his peers and his weight of 34.9 kg was near the mean for his age category.

Discussion

In studying age- and sex-specific changes in chimpanzees from a large colony housed at a single facility, we observed that IGF-1 levels increased rapidly at similar rates in males and females throughout childhood, peaked at puberty, then declined more slowly through adulthood, although faster in males than in females. Although we cannot directly compare IGF-1 values observed in this cohort with those found in humans because of differences in assays and the lack of a human comparator in our study, we did consider that the observed pattern of changes in chimpanzees largely recapitulates patterns observed in humans, albeit with several distinctions.

In a study of more than 15 000 human subjects, IGF-1 levels were slightly but significantly higher in males than in females in all age categories [7]. By contrast, we observed higher mean IGF-1 levels in males than in females only when all ages were pooled. We observed no differences in IGF-1 levels between males and females within their respective age categories. However, higher IGF-1 levels were reported in female juvenile and adolescent chimpanzees (including pubertal chimpanzees) vs males in the same age groups [8]. It is possible that the relatively smaller cohort size of each age category of chimpanzees vs humans makes it difficult to accurately assess sex-specific differences.

Female chimpanzees in our cohort exhibited peak IGF-1 levels between the ages of 5 and 8 years, while male levels peaked between the ages of 7 and 9.2 years. Similar cutoff points for pubertal IGF-1 levels were noted in other chimpanzee cohorts [8]. Although absolute values in humans are different, the pattern of IGF-1 levels peaking earlier in females than in males is similar [7, 14]. We observed a slightly wider peak in females than in males (3 vs 2.2 years, respectively), and similar pattern of a broader IGF-1 peak in females vs males is seen in humans [7, 14].

In humans, up until the age of 80 years, males show slightly higher IGF-1 levels than do females; after age 80, IGF-1 levels are slightly lower in males vs females [7]. Although we observed numerically similar IGF-1 levels in male and female elderly chimpanzees aged >35 years, the small numbers within this age category precluded meaningful analysis of the differences between the sexes. Moreover, the lack of robust studies of chimpanzees aged >35 years makes it difficult to know whether they are representative of humans aged >80 years.

Another approach to evaluating IGF-1 levels is by calculating the slope, or rate of change over time. Until the pubertal peak, the rate of the IGF-1 level increase was similar in males and females; thereafter, they diverged significantly, decreasing faster in males than in females. Comparison to humans is difficult, as, to our knowledge, no studies have reported IGF-1 slopes in both males and females. One study showed that IGF-1 levels declined by 40% among 300 males between the ages of 20 and 86, with a slope of -1.8, and this decrease correlated with age (r -0.6, $P < 0.0001$) [15]. However, females were not included in this cohort nor were IGF-1 slopes reported in larger studies of human subjects [7].

We observed higher PRL levels across all ages among females than males, as also observed in humans [16]. However, unlike in humans [17], PRL levels in chimpanzees continually increase with age; this rate of increase is approximately 4-fold steeper in females. Interindividual differences were notably large, as previously observed in both humans [15] and chimpanzees [5], likely resulting from multiple possible sources of circulating PRL, including endogenous sources (pituitary gland, inflammatory cells) and exogenous sources (medications), as well as the effect of

fluctuating sex hormone levels in females during the menstrual cycle [18]. It is also possible that manual or oral nipple stimulation to elicit milk, a behavior observed in postpartum female chimpanzees, contributed to the PRL variation [19]. Four females exhibited very high PRL levels, above the standard curve for our assay, and as re-assay with dilution was not possible, they were excluded from analysis. The cause of PRL elevations in 3 of these 4 females was likely continuous nursing. The 4th female, who was not nursing, was very obese.

We recognize that our sample size, although large for chimpanzees, is too small to determine population-based reference intervals, especially for individual age groups. Further, serum samples were all obtained from a single cohort of chimpanzees housed at a single facility, and differences in age at menarche and 1st gestation, interbirth intervals, and lifetime reproductive success between facilities and between captive and wild chimpanzees have been reported [20]. We also do not have documentation on Tanner-type stages of sexual development, chimpanzee height, comorbidities, and concomitant medications, or menstrual status, all of which influence the accurate assessment of hormonal levels. Therefore, the normal ranges we observed in each group may not be directly applicable to all chimpanzees.

Nevertheless, we successfully applied these results to establish normative values for this colony and to identify 2 pubertal males with low IGF-1. One male, A6A001, had clinical signs suggestive of GH deficiency, and our documented IGF-1 deficiency supported the diagnosis. Autopsy findings showed a midbrain malformation, indicating a likely cause for the disorder. The other male, A5A008, did not have features suggestive of GH deficiency, and was not genetically related to A6A001. It is therefore unclear whether the low IGF-1 indicates GH deficiency or simply delayed puberty. His dam was reported to be inattentive after his birth and he was placed in the nursery for a year, but the clinical significance of his low IGF-1 level is unknown. Of note, PRL levels in these 2 males were similar to the rest of their age group, further highlighting that multiple sources contribute to measures of circulating PRL independent of pituitary hormone secretion.

In conclusion, we developed a set of normative values for IGF-1 and PRL levels for a large colony of chimpanzees and confirmed suspected GH deficiency in 1 male chimpanzee with short stature and identified a 2nd male with delayed puberty. IGF-1 levels over the lifespan recapitulate changes seen in humans. As in humans, we observed steep increases during childhood in chimpanzees and a peak in puberty at an earlier age in females than in males, then slow declines thereafter throughout adulthood, although IGF-1 levels decline faster in male than in female chimpanzees. By contrast, patterns of PRL level changes in chimpanzees over the lifespan are less similar to those in humans. Like in humans, PRL levels are higher in female than in male chimpanzees but, unlike in humans, levels steadily increase with age in both sexes. Establishing normative IGF-1 and PRL levels in chimpanzees will allow better understanding of their health and maturity and provide a needed tool to diagnose rare hormone abnormalities such as GH and/or pituitary deficiency. In addition, as *IGF1* and *PRL* genes are highly conserved between humans and chimpanzees, comparing patterns of IGF-1 and PRL may shed light on maturity and hormone disorders in humans.

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