Comparative Medicine
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Vol 61, No 5
October 2011
Pages 457–461

Original Research

Morphometric Variables Related to Metabolic Profile in Captive Chimpanzees (*Pan troglodytes*)

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Obesity is a risk factor for several diseases including type 2 diabetes and cardiovascular disease. The aim of this study was to compare the relationships of waist circumference and body weight with circulating markers of metabolic, cardiovascular, and hepatic function in chimpanzees (*Pan troglodytes*). After a 12-h fast, blood was collected from 39 adult captive chimpanzees for measurement of serum glucose, BUN, creatinine, albumin, cholesterol, ALT, AST, ALP, total and direct bilirubin, triglyceride, and insulin, and waist circumference and body weight were measured. Waist circumference was positively correlated with systolic and diastolic blood pressure, glucose, insulin resistance as estimated by the homeostatic model assessment method, and albumin in female chimpanzees and with triglyceride in female and male chimpanzees. Body weight was correlated significantly with systolic and diastolic blood pressure in female chimpanzees and triglyceride in male chimpanzees. Male chimpanzees were heavier and had lower diastolic blood pressure, greater creatinine, albumin, AST, ALP, total bilirubin, and direct bilirubin values than did female chimpanzees. The relationships between waist circumference and blood pressure and triglyceride are consistent with those reported in humans and other primate species. In conclusion, our study is the first work to demonstrate a relationship between waist circumference and metabolic risk factors in chimpanzees. Results demonstrated that waist circumference was associated with more metabolic risk factors than was body weight, particularly in female chimpanzees.

Abbreviation: HOMA–IR, insulin resistance as estimated by homeostatic model assessment method.

Excess storage of body fat, known as obesity, leads to multiple health problems. Disorders such as cardiovascular disease, type 2 diabetes, arthritis, cancer, and mechanical joint trauma all are related to obesity.[36] In humans and nonhuman primates, obesity is associated with hypertension, insulin resistance, hyperglycemia, hypertriglyceridemia, hypercholesterolemia, and alterations in hematologic and serum chemistry values.[1,2,6,9,20,26,28,35,38,41] Significant sex-associated differences have been described in the relations between body fat and metabolic markers in humans. For example, despite having higher body fat percentages, women had lower concentrations of serum lipids than did men.[8] Although the effects of age and sex on these relationships have been described to occur in some nonhuman primate species,[30] other species have largely been understudied.

Assessments of obesity and type 2 diabetes have been made across several species, including humans and nonhuman primates.[3,16,19,29,31,32,38,40] Laboratory nonhuman primates show various features of human obesity, for example glucoregulatory impairments, hyperlipidemia, and changes in androgen concentrations.[31] Like humans, nonhuman primates are likely to develop obesity in adulthood,[23] manifesting primarily as excess abdominal adiposity. Obesity is now considered a major health problem for captive primates.[37] In particular, obesity is recognized as a problem among captive chimpanzees (*Pan troglodytes*), but these observations are largely underreported.[38]

Obesity has been defined by using many criteria.[31] Body fat estimation by using morphometric techniques is inexpensive and noninvasive.[29] Waist circumference has been used as a sensitive index of total body fat in nonhuman primates and can be easily and accurately measured.[23]

The objective of the study presented here was to investigate the relationship between the simple morphometric measurements of waist circumference and body weight and circulating markers of metabolic, cardiovascular, and hepatic function in chimpanzees.

Materials and Methods

Animals. The subjects were 39 clinically normal adult male (n = 17; age, 21.8 ± 7.2 y) and female (n = 22; age, 23.8 ± 10.9 y) chimpanzees (*Pan troglodytes*) housed at the Southwest National Primate Research Center (San Antonio, TX), an AAALAC-accredited facility at the Texas Biomedical Research Institute. The protocol was approved by the IACUC of the Texas Biomedical Research Institute.

Animal management. The population is organized into 55 compatible social groups of 2 to 5 chimpanzees, housed with indoor–outdoor access in standard stainless steel cages with covered shelters and equipped with external containers for food and ad libitum access to water. The animals' diets included commercial chow (Monkey Diet 15% 5LEO, Purina LabDiet, Brentwood, MO)

Received: 24 Feb 2011. Revision requested: 04 Apr 2011. Accepted: 15 Jul 2011.
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supplemented with seasonal fresh fruits and vegetables twice daily. They also received varied food enrichment throughout the day (that is, grains, fruits, vegetables, cereals, and frozen juice). Social rankings were grouped into levels of low, medium, and high and focused on the degree of aggressive dominance relationships within each troop. These rankings were determined by a trained member of the facility behavioral staff.

Physical examinations were performed for health assessment, including blood pressure, heart conditions through electrocardiography, cardiac and respiratory frequencies, abdominal palpation, auscultations of heart and lung murmurs, and mucosal exams (nasal, oral, and vaginal). In addition, feces and blood were collected at this time. Animals underwent tuberculin testing in the upper eyelid (0.1 mL, Tuberculin Mammalian, Human Isolates, Intradermic, Coopers Animal Health, Kansas City, KS) and were vaccinated periodically against pneumococcal infections and diphtheria, pertussis, and tetanus. Blood pressure was measured by using a blood pressure monitor (Prodigy II 2200, Omron Colin Medical, San Antonio, TX). The blood pressure cuff was placed on the arm (between shoulder and elbow), with the animal in dorsal recumbence. A minimum of 4 separate readings were taken at 1-min intervals, and the average diastolic and systolic pressures were recorded. Electrocardiography was performed (MAC 1200, GE Medical Systems, Milwaukee, WI). Fasted whole-blood samples were collected over 12 h from the femoral vein into vacuum phlebotomy tubes (Becton Dickinson Vacutainer Systems, Franklin Lakes, NJ). Plasma samples were collected in EDTA anticoagulant tubes. Fasted chimpanzees were anesthetized by using tiletamine–zolazepam (dose, 3.0 to 4.0 mg/kg; Telazol, Fort Dodge, IA) combined with xylazine hydrochloride (dose, 0.25 to 0.5 mg/kg; Rompun, Fort Dodge Animal Health).

Chimpanzees are trained to present body parts (that is, arms, legs, flank) for intramuscular injection, blood sampling, clinical treatment, or procedures.

Morphometric measures. During each chimpanzee's physical examination, total body weight (kg) and waist circumference (cm) were measured. Body weight was measured by using a digital floor scale (Tristar Metals, Boyd, TX). Waist circumference was measured at the midpoint between the lowest rib and the iliac crest by using a calibrated measuring tape.

Clinical chemistries. Serum chemistries were analyzed according to standardized methods as previously reported[12,15] for the components glucose, BUN, creatinine, albumin, cholesterol, ALT, AST, ALP, total bilirubin, direct bilirubin, and triglyceride. Analyses were performed on an automated analyzer with an attached ion-selective electrode module (Cobas Mira, Roche, Diagnostic Systems, Nutley, NJ). Insulin was measured by using the ultrasensitive human insulin-specific radioimmunoassay (Millipore, Billerica, MA). An estimate of insulin sensitivity was obtained by using the homeostasis model assessment—insulin resistance (HOMA–IR) equation:

$$\text{Insulin (IU/mL)} \times \text{glucose (mmol/L)} / 22.5.^{27}$$

Statistical analysis. Sex-associated differences in metabolic variables and morphometric measurements were determined by using independent-samples *t* tests. Metabolic parameters were log-transformed, wherever necessary, to normalize their distributions. Pearson correlation coefficients were used to evaluate relations among variables. Statistical significance was set at a *P* value of less than 0.05. All statistical analyses were performed by using SyStat software version 12 (SyStat, Chicago, IL).

Results

Male chimpanzees were heavier and had lower diastolic blood pressure and higher levels of circulating creatinine, albumin, AST, ALP, and total and direct bilirubin than did female chimpanzees (Table 1). Waist circumference was positively correlated with systolic and diastolic blood pressure, glucose, HOMA-IR, and albumin in female chimpanzees, whereas triglyceride was correlated with waist circumference in both sexes (Table 2). Body weight was significantly ($P < 0.05$) correlated with serum glucose and systolic and diastolic blood pressure in female chimpanzees and triglyceride in male chimpanzees (Table 2). The serum AST level was significantly correlated with cholesterol ($r = 0.684$, $P = 0.002$) in male chimpanzees and with albumin ($r = -0.531$, $P = 0.011$) in female chimpanzees; ALT was positively correlated with triglyceride in female chimpanzees ($r = 0.519$, $P = 0.013$). No significant correlations were observed between ALT or AST levels and blood pressure, glucose, insulin, HOMA-IR, and ALP. In addition, no significant correlations were found between the social dominance rankings and analyzed metabolic factors.

Discussion

A series of body size measurements including waist circumference and body weight comprise the anthropometric methods used in human research.[29] Given the need to assess adiposity in captive chimpanzees in a simple and effective manner, we undertook the current study to determine whether waist circumference and body weight were accurate correlates of metabolic risk factors in these animals. In contrast to body weight, waist circumference was associated with several metabolic risk factors in female chimpanzees including fasting glucose, HOMA-IR, triglyceride, and blood pressure. Both waist circumference and body weight were correlated with triglyceride in the male group. Our findings suggest that waist circumference can serve as a useful indicator of metabolic health in captive chimpanzees.

We found significant body weight variation between sexes, consistent with findings in other studies.[38] These differences may result from genetic variation (which is attributable to genetic factors), nutrition, physical activity, and environmental stress conditions, such as infectious disease and social conflict.[39] Consistent with our findings, adult captive nonhuman primates usually weigh more than their free-ranging counterparts.[25] In captivity, animals that are socially dominant have preferential access to food and spend longer periods of time at feeding sites.[31] Obese animals often come from high-ranking natal families.[34] However, we noted no significant correlation between body weight or waist circumference and social rank in our study.

The extent of central adiposity in humans often is approximated by using waist circumference. Increased fasting insulin is indicative of insulin resistance and is a key feature of the cardiometabolic syndrome.[7] In humans, abdominal fat deposition is associated more strongly with type 2 diabetes as well as hypertension and cardiovascular disease than is fat accumulation in the hips and thighs.[33] Obese humans with excess abdominal fat are hyperinsulinemic and hypertriglyceridemic relative to their lean counterparts.[33] The strong correlations between waist circumference and metabolic risk factors in the female chimpanzees in our study likely reflect the effects of abdominal adiposity. In the male chimpanzees in our study, the correlations of abdominal adiposity with waist circumference were similar in magnitude to those with body weight. Moreover, only fasting triglyceride

Table 1. Sex-associated differences in metabolic variables of chimpanzees

	Female (n = 22)			Male (n = 17)			
	mean ± 1 SD	Expected range	95% confidence interval	mean ± 1 SD	Expected range	95% confidence interval	P
Age (y)	23.8 ± 10.9	—	19.25–28.34	21.8 ± 7.2	—	18.3–25.2	0.487
Waist circumference (cm)	83.7 ± 10.1	—	79.4–87.9	81.0 ± 5.4	—	78.5–83.6	0.306
Body weight (kg)	58.1 ± 9.8	—	50.4–65.7	66.9 ± 8.9	—	62.7–71.2	*0.005*
Systolic blood pressure (mm Hg)	134.4 ± 16.8	—	127.3–141.4	134.6 ± 22.9	—	123.7–145.5	0.966
Diastolic blood pressure (mm Hg)	67.2 ± 13.4	—	61.6–72.8	55.4 ± 13.2	—	49.1–61.7	*0.010*
Glucose (mg/dL)	124.0 ± 20.2	64–100	115.5–132.5	111.9 ± 17.2	45–119	103.8–120.1	0.052
Insulin (μU/dL)	9.2 ± 4.1	—	7.10–11.2	10.1 ± 7.4	—	6.6–13.6	0.646
HOMA–IR	2.8 ± 1.6	—	2.3–3.3	2.7 ± 1.6	—	2.2–3.2	0.819
BUN (mg/dL)	8.5 ± 2.2	5–23	7.6–9.4	9.1 ± 1.4	5–15	8.5–9.8	0.283
Creatinine (mg/dL)	0.9 ± 0.2	0.3–1.1	0.88–1.08	1.2 ± 0.2	0.5–1.3	1.08–1.25	*0.010*
BUN:creatinine	8.9 ± 2.1	—	8.0–9.7	8.0 ± 1.7	—	7.2–8.8	0.166
Albumin (g/dL)	3.3 ± 0.3	3.0–3.8	3.2–3.4	3.6 ± 0.2	3.1–4.1	3.5–3.7	*0.006*
Cholesterol (mg/dL)	195.1 ± 40.4	152–314	178.2–212.0	180.9 ± 28.7	135–269	167.2–194.5	0.206
ALT (U/L)	28.1 ± 6.4	21–55	25.4–30.8	38.1 ± 18.9	25–53	29.1–47.0	0.051
AST (U/L)	21.5 ± 7.3	11–25	18.5–24.6	33.9 ± 12.2	2–48	28.2–39.7	*0.001*
ALP (U/L)	66.1 ± 18.4	0–703	58.4–73.8	87.3 ± 23.0	0–892	76.3–98.2	*0.004*
Total bilirubin (mg/dL)	0.1 ± 0.1	0.1–0.3	0.096–0.194	0.3 ± 0.1	0.1–0.5	0.21–0.35	*0.004*
Direct bilirubin (mg/dL)	0.01 ± 0.03	0.1–0.3	0.0003–0.03	0.1 ± 0.1	0.1–0.3	0.037–0.127	*0.010*
Triglyceride (mg/dL)	63.7 ± 26.1	29–133	52.8–74.6	73.6 ± 35.8	30–102	56.5–90.6	0.345

HOMA–IR, homeostasis model assessment—insulin resistance.
Italics indicate parameters showing statistically significant ($P < 0.05$) differences between sexes.

Table 2. Correlation (r value) of waist circumference and body weight with metabolic indicators in male and female chimpanzees

	Waist circumference		Body weight	
	Male (n = 17)	Female (n = 22)	Male (n = 17)	Female (n = 22)
Systolic blood pressure (mm Hg)	−0.165 (0.526)	*0.648 (0.001)*	0.027 (0.918)	*0.658 (0.001)*
Diastolic blood pressure (mm Hg)	0.346 (0.174)	*0.640 (0.001)*	0.289 (0.260)	*0.627 (0.002)*
Glucose (mg/dL)	−0.211 (0.416)	*0.433 (0.044)*	−0.293 (0.254)	*0.402 (0.002)*
Insulin (μU/mL)	0.265 (0.303)	0.390 (0.073)	0.061 (0.816)	0.126 (0.576)
HOMA–IR	0.192 (0.460)	*0.514 (0.014)*	−0.032 (0.904)	0.255 (0.252)
BUN (mg/dL)	0.282 (0.273)	0.061 (0.788)	0.206 (0.427)	0.041 (0.858)
Creatinine (mg/dL)	0.309 (0.228)	−0.192 (0.391)	0.318 (0.213)	−0.047 (0.836)
BUN:creatinine	−0.022 (0.932)	0.267 (0.230)	−0.083 (0.752)	0.106 (0.638)
Albumin (g/dL)	−0.079 (0.762)	*0.428 (0.047)*	−0.043 (0.869)	0.391 (0.072)
Cholesterol (mg/dL)	−0.021 (0.938)	0.181 (0.419)	0.161 (0.538)	−0.084 (0.711)
Triglyceride (mg/dL)	*0.599 (0.011)*	*0.431 (0.045)*	*0.504 (0.039)*	0.350 (0.110)
ALT (U/L)	−0.107 (0.683)	0.222 (0.320)	−0.176 (0.500)	0.138 (0.540)
AST (U/L)	0.076 (0.811)	−0.003 (0.991)	−0.076 (0.772)	0.059 (0.795)
ALP (U/L)	0.095 (0.715)	0.166 (0.461)	−0.068 (0.795)	0.207 (0.356)
Total bilirubin (mg/dL)	0.326 (0.202)	0.127 (0.572)	0.287 (0.263)	0.089 (0.692)
Direct bilirubin (mg/dL)	0.191 (0.462)	−0.042 (0.851)	0.435 (0.081)	−0.128 (0.571)

HOMA-IR, homeostasis model assessment—insulin resistance.
Italics indicate statistically significant ($P < 0.05$; in parentheses) correlation between the parameters evaluated.

concentrations were correlated with morphometrics in the male chimpanzees studied. Similar findings were reported in a previous study,[38] in which morphometric measures were unrelated to circulating biomarkers in male but not female chimpanzees. As in the cited study,[38] the male chimpanzees in our study were largely metabolically healthy. Validated body weight standards or similar references are not available for defining overweight or obesity in chimpanzees.

Our data suggest that compared with body weight, waist circumference is a better indicator of the metabolic disease risk measures such as blood pressure, HOMA-IR and serum levels of glucose, albumin, and triglycerides in female chimpanzees.

Body weight was significantly associated with fasting triglyceride in male but not female chimpanzees. However, as noted earlier, neither body weight nor waist circumference was correlated with any of the other metabolic variables in male chimpanzees. In contrast to body weight, waist circumference was associated with fasting glucose, HOMA-IR, and triglyceride in female chimpanzees in our study. Body weight and waist circumference were correlated similarly with blood pressure in female chimpanzees. Our findings are consistent with the notion that waist circumference can serve as a useful morphometric for assessing metabolic health in captive chimpanzees. Waist circumference may be a better indicator of metabolic status than is body weight, at least in female chimpanzees. Nevertheless, further studies in overweight and obese male chimpanzees are warranted.

In line with other findings[5,38,39] we found that male chimpanzees were significantly heavier than similarly aged females, reflecting a sexual dimorphism that is common among nonhuman primate species. However, male and female chimpanzees had similar waist circumference in our study; given that the female chimpanzees had a smaller body size, these data suggest that they had greater relative adiposity. Female chimpanzees had higher diastolic blood pressure and modestly higher fasting serum glucose concentrations. However, other hallmarks of metabolic status—namely HOMA-IR, fasting insulin, and triglyceride—did not differ between the sexes. We conclude that the higher blood pressure and glucose concentrations of female chimpanzees may have been attributable to their greater adiposity.

Like humans, nonhuman primates have a tendency to become obese during adulthood.[23] Obese nonhuman primate are hyperlipidemic[13,22] and presumably at risk for hypertension and cardiovascular disease. High concentrations of serum albumin have been associated with cardiovascular risk in humans.[11,24] In addition, cardiovascular disease is positively associated with increased waist circumference in humans.[21] In our study, we found a positive association between waist circumference and serum albumin in female but not male chimpanzees. Renal function-related serum biomarkers (that is, BUN and creatinine concentrations) have been shown to be significantly lower in adult female than male chimpanzees.[18]

In baboons, sex-associated differences in muscle mass are reflected by the higher plasma creatinine concentrations observed in male compared with female chimpanzees.[14] The higher creatinine of the male chimpanzees in our current study is likely similarly attributable to their greater muscle mass.

Circulating concentrations of the hepatic enzymes ALT and AST are indicative of liver function and are related to nonalcoholic fatty liver disease.[18] Previous reports have stated that the activities of ALT and AST are significantly lower in adult female than male chimpanzees.[17,18] This result is consistent with our findings, in which AST was significantly lower and ALT was modestly lower in female compared with male chimpanzees. Studies conducted in baboons have shown that AST concentrations, fat cell volume, and body weight are influenced by a common set of genes.[4] In addition, sex-associated differences in the levels of AST and bilirubin may be related to the effects of the menstrual cycle and perineal cycle in female baboons.[14] Because we did not have reproductive-related phenotypes for this study, we could not assess these putative effects. Additional noteworthy findings are that we detected strong relationships between ALT and triglyceride in female chimpanzees and between AST and cholesterol in male chimpanzees. These findings may indicate that fasting triglyceride is a good indicator of hepatic function in chimpanzees.[10]

In conclusion, our current study is the first to demonstrate a relationship between waist circumference and metabolic risk factors in chimpanzees. Our results suggest that waist circumference is a better indicator of metabolic health than is body weight, particularly in female chimpanzees. These results provide information that can be used for improving animal management in regard to diet, physical activity, and other environmental factors, with the goal of reducing cardiometabolic disease in captive chimpanzees. In addition, due to the evolutionary proximity and similar phylogenetic characteristics of chimpanzees and humans, the metabolic patterns we uncovered in chimpanzees can be extrapolated to humans and contribute to the understanding of human metabolic disorders.

Acknowledgments

We thank David Pineda, Nancy Martin, Jose Vallejo, and Daniel Alonzo for their invaluable technical assistance with this study. We also thank Maribel Vazquez for providing the behavioral status data of the chimpanzees. The research was supported by CAPES and NIH grants P51 RR013986, C06 RR014578, and C06 17515.

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