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Sexual and Hormonal Cycles in Geriatric *Gorilla gorilla gorilla*

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As our closest living relatives, great apes likely experience behavioral and physiological patterns associated with reproductive aging and menopause that are similar to human patterns. We present results from a nationwide zoo-based study on behavioral and hormonal changes in female western gorillas. We evaluated progestogen concentrations via daily fecal sampling in 30 gorillas, 22 of which were geriatric (≥30). We collected concurrent behavioral data 1–3 times weekly on 16 of the females. While control females cycled regularly, ca. 23% of geriatric females are acyclic (menopausal), and another 32% show variable hormonal patterns suggesting perimenopause. Patterns included increased variability in cycle length and peak progestogen values, and frequent insufficient increases in progestogen levels during the luteal phase. Acyclic females have significantly lower overall progestogen concentrations than the self cycling females, though differences are not significant when cycle phase is incorporated. We detected behavioral estrus in 9 of 10 cycling females for which data were available. In all but 1 case, proceptive behavior occurred during the follicular phase, preceding ovulation on average by 6.6 d. Females spent more time in proximity to the silverback male while in behavioral estrus than during other periods. To date, maximum longevity in captive female gorillas is 52 yr, with poor reproductive prognosis beginning from the age of 37. We demonstrate that both perimenopause and menopause characterize aged female gorillas, which

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may experience a postreproductive lifespan of >25% of their lives. Continued study of aging apes is warranted, and apes may serve as models for age-related reproductive changes in humans.

KEY WORDS: geriatric; gorilla; menopause; perimenopause.

INTRODUCTION

What role can nonhuman primates serve as we investigate human reproductive aging? Researchers have proposed that aged nonhuman primates can provide valuable insights into the clinical symptoms of menopause, a particularly distinctive phase of reproductive aging in human females, in addition to answers concerning the evolutionary significance of the phenomenon (Archer, 2004; Bellino, 2000; Gould *et al.*, 1981; Graham, 1981; Kaplan, 2004; Schramm *et al.*, 2002). To date, related research has focused primarily on macaques (Gilardi *et al.*, 1997; Graham *et al.*, 1979; Johnson and Kapsalis, 1998; Pavelka and Fedigan, 1999; Schramm *et al.*, 2002; Shideler *et al.*, 2001; Small, 1984; Takahata *et al.*, 1995; Walker, 1995), with few data from other monkey species (Borries *et al.*, 1991; Dolhinow *et al.*, 1979; Harley, 1990; Sommer *et al.*, 1992; Strum and Western, 1982; Tardif and Ziegler, 1992; Waser, 1978). Surprisingly, primatologists have investigated ape species markedly less well, though long lifespans, large body sizes, slow life history traits, and close taxonomic ties with humans may make them more suitable paradigms for research on reproductive aging in humans. Researchers have conducted numerous cross-sectional reproductive hormonal studies, but they are often based only on 1 or 2 menstrual cycles of nonaged female apes (Bellem *et al.*, 1995; Czekala *et al.*, 1991; Dahl *et al.*, 1987; Graham, 1979; Jurke *et al.*, 2001a,b; Lasley *et al.*, 1982; Mitchell *et al.*, 1982; Miyamoto *et al.*, 2001; Nadler, 1975, 1980; Vervaecke *et al.*, 1999). Available data from aged chimpanzees and bonobos regarding cycling at advanced ages have not yielded consistent results; some geriatric individuals cycle regularly, while others cease cycling in the years before death (Goodall, 1986; Graham, 1979; Jurke *et al.*, 2000; Nishida *et al.*, 2003). Data on aging orangutans and gorillas are even fewer. There are reported cases of orangutan females giving birth at an advanced age (Wich *et al.*, 2004), while the opposite is true for mountain gorillas (Stewart *et al.*, 1986). Given the paucity and variability of available information, there was a need for more data on reproductive senescence in aging female apes; thus we report results of hormonal and associated sexual cycling patterns from a nationwide study on aging female western gorillas (*Gorilla gorilla gorilla*) housed in zoos across North America.

We began with a pilot study at Brookfield Zoo, in which we compared hormonal cycles, as measured via fecal progestogens, of a >40-yr-old female to sexual behaviors exhibited monthly toward the silverback male (Atsalis *et al.*, 2004). The aged female had regular progestogen peaks that followed proceptive behavior, but her cycles were longer than those of a younger control female. We were uncertain how widespread the pattern was among aged gorillas because no other study had focused on aged gorilla subjects. As near relatives to humans, gorillas can be valuable conceptual models for understanding human reproductive aging (Stewart *et al.*, 1986). Similarities exist between the 2 species. In common with human females, gorillas, like the other apes, but unlike monkeys, are nonseasonal breeders (Stewart *et al*., 1986). Like other nonhuman primates, gorillas demonstrate an obvious behavioral estrus, but, unlike chimpanzees and bonobos, the labial swellings associated with reproduction are extremely subtle (Furuichi, 1987; Graham, 1981), and may play less of a role in reproductive behavior (Harcourt *et al.*, 1980). Moreover, gorillas and humans display physiological similarities in monthly fluctuations of reproductive hormones (Graham, 1981; Loskutoff *et al.*, 1991), though Loskutoff and coworkers also noted a double follicle-stimulating hormone (FSH) peak in gorillas, compared to the single peak in humans. Finally, in contrast to female chimpanzees and orangutans which are often alone or only with offspring, gorilla females, like human females, are habitually in close social group contact with a breeding male (Watts, 1991).

Considerable controversy surrounds the question of whether menopause characterizes nonhuman primate species (Alvarez, 2000; Austad, 1994; Hawkes, 2003; Hawkes *et al.*, 2003; Hill and Hurtado, 1991; Mayer, 1982; Pavelka and Fedigan, 1991; Peccei, 2001a,b; Rogers, 1993). Clinically, menopause is defined as the permanent cessation of menstruation that results from losing ovarian follicular function (Burger *et al.*, 1995). However, some evolutionary anthropologists assert that an extended lifespan after termination of reproduction is a special attribute of the human menopause (Pavelka and Fedigan, 1991), because only human females can expect to live a third or more of their lives postreproductively (Hill and Hurtado, 1991; Pavelka and Fedigan, 1991; Peccei 2001a,b; Stanford *et al.*, 1987). Accumulating evidence from captive individuals, and from long-term studies in the wild, affirms that there are postmenopausal nonhuman primate females (Borries *et al.*, 1991; Nishida *et al.*, 2003; Small, 1984; Sommer *et al.*, 1992; Strum and Western, 1982; Waser, 1978), but their postreproductive lifespans are short compared to those of humans (Caro *et al.*, 1995; Hawkes *et al.*, 1998; Pavelka and Fedigan, 1991). Moreover, with the exception of humans, reproductive cessation does not appear to occur universally in any other primate species studied. Because of these

crucial differences, some investigators now maintain that nonhuman primate females are of limited use for understanding human reproductive termination (Martin *et al.*, 2003).

Nevertheless, the many similarities between aging nonhuman and human females provide ample justification for continued focus on nonhuman primate females as they age. Under captive conditions, nonhuman primates are living longer, reaching maximum lifespans, and are more likely to experience complete cessation of reproduction years before death (DeRousseau, 1994). Like humans, many nonhuman primate females experience decreased age-specific fecundity for several years before reproductive senescence (Gilardi *et al.*, 1997; Hodgen *et al.*, 1977; Johnson and Kapsalis, 1998; Kuester *et al.*, 1995; Nozaki *et al.*, 1995; Paul and Kuester, 1988; Paul *et al.*, 1993; Small, 1984; Tardif and Ziegler, 1992; Walker, 1995). Moreover, as with human females, aged nonhuman primate females can continue to cycle even as they experience advanced age infertility (Nozaki *et al.*, 1995; Takahata *et al.*, 1995; Wolfe and Noyes, 1981). Most notably, an increasing number of primate researchers are realizing that amplified variability in cycle lengths, and declines in fecundity with associated changes in hormonal secretions—symptoms exhibited before complete cessation of cycling—strongly parallel clinical symptoms of perimenopause in humans (Black and Lane, 2002; Downs and Urbanski, 2004; Erwin *et al.*, 2002; Gilardi *et al.*, 1997; Gould *et al.*, 1981; Graham, 1979; Hodgen *et al.*, 1977; Jensen *et al.*, 1982; Johnson and Kapsalis, 1998; Nozaki *et al.*, 1995; van Wagenen, 1972; Walker, 1995; Weiss, 2001). Consequently, whatever the limitations of nonhuman primates as paradigms for understanding postmenopausal events, they can be suitable models for investigating other important aspects of reproductive aging such as the perimenopause (Martin *et al.*, 2003).

Declines in fecundity with advanced age characterize wild mountain gorillas (Stewart *et al.*, 1986) as well as captive western ones (Wharton and Thompson, 2000). Demographic information from the captive gorilla population points to a combination of longevity and reduced fecundity in females as they age (Wharton and Thompson, 2000). These observations and those from our pilot study, in which longer and more variable cycle lengths occurred in older individuals, led us to suggest that gorillas may experience a perimenopause (Atsalis *et al*., 2004). In humans, the perimenopause is associated with decreased progesterone secretion and shorter follicular phases (Santoro *et al.*, 1996; Weiss, 2001). Therefore, we compared progestogen concentrations and cycle lengths between older and younger gorilla females and report on associated sexual behaviors. We identify postreproductive females and investigate perimenopausal symptoms in geriatric females via examination of current hormonal patterns and by comparing the presence of

sexual behavior and contact with the silverback with patterns in hormonal cycling. We use the measures as an alternative to the commonly applied *time lag from last birth* criterion (Caro *et al.*, 1995; Nishida *et al.*, 1990; Paul *et al.*, 1993; Takahata *et al.*, 1995) because the high degree of interindividual reproductive variability that characterizes captive gorillas makes the criterion even less desirable than suggested for other primates (Pavelka and Fedigan, 1999).

Field data on age-related changes associated with female ape reproduction are few, partially as a result of the difficulties involved in long-term monitoring of long-lived species, and because of the challenge in estimating the age of study subjects. Conversely, in the captive population, ages and reproductive histories of females are known; the zoo-based investigation is particularly timely because the number of elderly gorillas in captivity is growing (Erwin *et al.*, 2002). Twenty-eight percent of captive western gorilla females (52 of 187 females) are considered geriatric, >30 yr, according to the North American Regional Studbook for western gorillas, while 17% (32 of 187 females, or 62% of geriatric females) are >35 yr old (Wharton, 2000). Primate gerontologists have called for more studies on aging apes, noting the need for long-term endocrine monitoring of aging apes to document reproductive senescence (Erwin *et al.*, 2002; DeRousseau, 1994). Given reports on reproductive failure in older gorilla females (Mitchell *et al.*, 1982; Thompson, *pers. commun.*; Wharton, *pers. commun.*), it is the opportune time to investigate how they experience age-related reproductive changes.

METHODS

For *ca.* 3 mo per subject we monitored progestogen concentrations via daily fecal collection, assessed estrus daily, and, with some exceptions, collected behavioral data ≥1 time/wk.

Subjects

The 30 subjects were captive western gorillas (*Gorilla gorilla gorilla*) from 17 North American zoos. The North American Regional Studbook for western gorillas considers individuals >30 yr old to be geriatric (Wharton and Thompson, 2000). With the exception of 2 females, 32 yr and 33 yr, we opted to be conservative in the analyses by choosing the stricter age limit of 35 yr because with the maximum lifespan of gorillas close to 52 yr—the current age of the longest lived captive gorilla—30 yr seemed relatively young to be considered geriatric. We obtained information on female reproductive

history via questionnaires sent to each zoological facility and from the gorilla studbook. Geriatric subjects were ≥35 yr and control females were 11–30 yr old. Females lived in a potentially breeding situation, i.e., with a silverback male, not pregnant, lactating, or on contraception during the study period, and ideally had experienced ≥1 pregnancy. The sample thus comprised 20 females ≥35 yr, 2 between 30 and 35 yr, and 8 between 11 and 30 yr—a total of 22 in the geriatric group and 8 in the control group (Table I). We had difficulty finding control females that were not pregnant, lactating, or on contraception. To include an adequate number of both geriatric and control subjects in the study, in a few cases we waived select criteria.

Behavioral Data

In gorillas, sexual behavior is demonstrated in an all-or-none fashion with estrus occurring within a narrow window of ≤2–3 d (Atsalis *et al.*, 2004; Harcourt *et al.*, 1980; Nadler, 1980, 1981; Stewart *et al.*, 1986). We checked females daily for estrous behaviors; we collected behavioral data during half-hour periods on the days that individuals exhibited estrus-related behaviors, and at least once weekly for nonestrus days. The reduced data collection schedule made the project accessible to a larger number of institutions with only a small risk of missing estrus. Overall, we collected behavioral data (Altmann, 1974) ≥1 time/wk for *ca.* 3 mo. We used instantaneous 2-min sampling to collect data on basic time budget activities—forage, rest, play, locomote, and autogroom—for later analysis, and to record distance from other group members (0 m, <1.5 m, 1.5–3 m, >3 m) to assess changes in proximity during behavioral estrus. We noted all instances of sexual behaviors on an all-occurrence basis, including touches, stares, and presentation positions directed toward the male, copulation, masturbation, and inspecting genitalia, as well as affiliative and aggressive behaviors, and approaches and withdrawals to and from the male and other group members. We included an all-occurrence category designated EO (estrus other) to cover additional estrous behaviors manifested. We gleaned additional information on individual gorilla sexual behavior from keeper assessments, particularly for females with subtle manifestation of sexual behavior.

To ensure interobserver reliability we provided on-site 2-d training for behavioral observations. The principal investigators had been working together collecting data at Brookfield Zoo for >1 yr. One of the principal investigators trained all data collectors at Brookfield Zoo and at other institutions until observations by the trainees and by the principal investigator coincided.

Table I. Description of subject females

Female/studbook no.	Institutution-Location of female	Birth date/age at time of study	Behavioral data collected	Number of live births	Last birth	Hormonal cycler[a]	Silverback	Special circumstances
Jenny (62)	Dallas Zoo	1953/51	Yes	1	1964	nc	Yes	Regular sexual relations with silverback until 2 yr ago.
Colo (56)	Columbus Zoo and Aquarium	1956/48	Yes	3	1971	c	Yes	
Trudy (73)	Little Rock Zoo	1957/47	Yes	1	1970's	c	Yes	
Shamba (221)	Zoo Atlanta	1959/46	Yes	at least 4	1989	nc	Yes	Silverback and female actively avoid each other.
Timbo (172)	Dallas Zoo	1962/42	Yes	0	NA	nc	Yes	Silverback never sired offspring.
Femelle (211)	Milwaukee County Zoological Gardens	1962/42	Yes	3	1992	c	Yes	
Alpha (159)	Brookfield Zoo	1961/41	Yes	7	1991	c	Yes	
Beta (160)	Brookfield Zoo	1961/41	No	2, possibly 3	1983	nc	No	Not housed with conspecifics
Choomba (180)	Zoo Atlanta	1963/41	Yes	3	1998	c	No	In all female group since silverback died in 2002.
Katanga (381)	Gladys Porter Zoo	1963/41	Yes	~6	1992	c	Yes	
Pongi (269)	Columbus Zoo	1963/41	Yes	3	1993	c	Yes	
Josephine (389)	Miami Metrozoo	1964/40	Yes	at least 1	1984	c	Yes	Shows little interest in silverback.
Linda (214)	Milwaukee County Zoological Gardens	1964/40	Yes	1	1979	c	Mesh access only.	
Ngajji (713)	Milwaukee County Zoological Gardens	1966/38	Yes	1	1980	c	Silvering blackback	
Elaine (300)	The Toledo Zoo	1966/38	Yes	1	1975	nc	Yes	Was surrogating a two-year old during the study.

Table I. Continued

Female/studbook no.	Institutution-Location of female	Birth date/age at time of study	Behavioral data collected	Number of live births	Last birth	Hormonal cycler[a]	Silverback	Special circumstances
Inaki (289)	Busch Gardens Tampa Bay	1967/37	No	0	NA	c	No	Housed with another female.
Haloko (393)	Smithsonian National Zoological Park	1967/37	Yes	4	1992	c	Yes	Silverback never sired offspring.
Donna (336)	North Carolina Zoological Park	1968/36	No	0	NA	c	Blackback	
Bibi (405)	Knoxville Zoological Gardens	1968/36	Yes	1	1975	c	Yes	
Sam (356)	Cincinnati Zoo and Botanical Garden	1970/35	No	7	1995	c	Yes	
Malaika (428)	The Toledo Zoo	1971/33	Yes	3	1994	c	Yes	
Kishina (456)	Busch Gardens Tampa Bay	1972/32	No	1	Pregnant	c	No	Initially housed with another female. Visits with male.
Hope (559)	North Carolina Zoological Park	1974/30	No	1	1989	c	Blackback	Housed with young males since 2000.
Babs (536)	Brookfield Zoo	1974/28	Yes	4	1991	c	Yes	Monthly proceptive behavior until onset of illness summer of 2004.
Juju (745)	Cheyenne Mountain Zoo	1980/24	Yes	3	1996	c	Yes	
Madge (759)	Cincinnati Zoo and Botanical Garden	1981/23	No	7	1997	c	Yes	
Muke (773)	Cincinnati Zoo and Botanical Garden	1981/23	No	2	1998	c	Yes	
Binti Jua (1047)	Brookfield Zoo	1988/16	Yes	1	Pregnant	c	Yes	
Kwizera (1044)	Buffalo Zoological Gardens	1988/16	No	1	1997	c	Yes	
Cassie (1303)	Columbus Zoo and Aquarium	1993/11	Yes	0	NA	c	Yes	

[a]nc indicates noncycling female; c is a hormonally cycling female as per results of this study.

Fecal Collection Protocol

For hormonal analysis, we collected feces instead of blood or urine because collection is easy and noninvasive. We collected daily fecal samples from each female for *ca.* 3 mo in conjunction with the behavioral observation schedule. To mark fecal samples we added 4 teaspoons (20 ml) of green food coloring daily to the subjects' food. For consistency, we used yellow food coloring for nontargeted individuals in a subject's social group, which did not mark feces. We collected 2–3-in pieces of same-day, fresh, fecal matter daily and stored them at –20°C until we sent the samples to Brookfield Zoo packed on dry ice.

Hormonal Assay Analysis

Before assay, we extracted .5-g aliquots of wet feces in 16×125 mm polypropylene test tubes with 5 ml of 80% ethanol in distilled water by shaking overnight (16–20 h) at room temperature on a Labline rotator (Fisher Scientific Hanover Park, IL). After we centrifuged the mixture for 15 min at 1500*g* in an EIC Marathon 3000R (Fisher Scientific, Hanover, IL), we added 1 ml of supernatant to 1 ml of assay buffer (.1 M phosphate buffered saline containing 1% bovine serum albumin [BSA], pH 7.0). We stored diluted extracts at -20°C until we continued with the assay process.

Brookfield Zoo's endocrinology laboratory conducted hormonal assay procedures (enzyme immunoassays [EIAs]), which are described in detail by Atsalis *et al.* (2004). Fecal hormonal analysis is restricted currently to steroid hormone metabolites, which for female reproductive hormones means predominantly progestogen and estrogen metabolites. As with bonobos (Jurke *et al.*, 2000) we found that fecal estradiol measurement was not meaningful for gorillas (Atsalis *et al.*, 2004). Gorilla estradiol cycles are highly variable and do not correlate with progestogen and behavioral cycles, suggesting that the assay was not specific enough to detect fecal metabolites of estradiol in the species, but progesterone hormone assays show cross-reactivity with several progestogen metabolites. Based on cycle length and correlation with behavior, progestogens in the fecal samples of gorillas proved to be more reliable indicators of cyclicity than estrogens were, and therefore we proceeded only with progestogen hormone analyses. For progestogens, intraassay and interassay coefficients of variation (CV) are 6.5% and 16.9% at 28.7% binding, and 8.5% and 22% at 66.5% binding, respectively. To evaluate plates for consistency, we monitored control samples for each assay for all subject females. Thus, the reported

interassay variation applies across the entire sample of control and subject females. The monoclonal P4 antibody is characterized by high variability; therefore, the CV for the assay is not unusual and is typical of other species as well (Bellem *et al.*, 1995; Schwarzenberger *et al.*, 1993). In conclusion, reported intra- and interindividual progestogen variability in the sample is indeed valid provided that it is >20%, which is the level of interassay variability indicated by the controls. Results are reported as ng/g of wet fecal matter.

Data Analyses

Hormonal Data Analyses

Baseline and Threshold Progestogen Concentrations. We calculated baseline and threshold values for progestogens to distinguish between follicular and luteal phases in female hormonal profiles and to determine estrus cycle lengths. Baseline value is essential to define the noncycling level of a species, and the common practice is to use the entire population for its calculation (Brown *et al.*, 2001). Therefore, to establish baseline progestogen level we combined hormonal data from all 30 subjects (2379 values), geriatric and control animals. We calculated baseline via an iterative process (Brown *et al.*, 2001) in which we excluded values that were outside the mean ±2.5 standard deviations (SD). We then recalculated the mean ±2.5 SD and repeated the exclusion process until all values outside of the mean ±2.5 SD were eliminated. Once we established baseline, we discovered that progestogen values across females were too variable for cycle phases to be adequately distinguished via only this value. Instead, we used a higher value or threshold, defined as the value that exceeded baseline by 50% (Brown *et al.*, 2001).

We omitted 1 noncycling geriatric female from analyses of progestogen concentrations because her values were a full order of magnitude higher than the ones for all other females, with an average of >7000 ng of progestogen/g of feces. Two other females, 1 geriatric and 1 control, had baseline progestogen concentrations higher than those of the other females. We recalculated their baseline and threshold values via a standard deviation of 2, rather than 2.5, so that lower baselines would not obscure obvious cycling patterns.

Cycle Lengths. In some instances, we used subjective observations to distinguish between differences in true cyclic changes in progestogen and random fluctuations in the data. For cycle lengths, we used Student *t*-test for comparison of means among groups, an *F* statistic to check for equality

of variance between sample groups, and in some cases, the CV to compare sample variability between sample groups. All statistical analyses are per Sokal and Rohlf (1981).

Estrus Cycle Lengths. The estrus cycle is based on fecal progestogen profiles. With the exception of 2 previously noted cases, we determined estrus cycle lengths based on the threshold value calculated for the entire sample. We defined onset of a luteal phase by the first points of a sustained progestogen increase (≥2 consecutive d) exceeding threshold (Brown *et al.*, 2001). We defined the end of the luteal phase as the first of 2 consecutive values that returned to threshold level. For each female, we defined estrus cycle lengths as the time between successive onsets of luteal phases. We used the data to determine average cycle length for geriatric and control subjects. The hormonal profiles of noncycling females lacked regular peaks displaying no sustained return to threshold concentrations, so that we were unable to determine cycle lengths. We calculated average peak progestogen values for each luteal phase and averaged them for the control ($n = 8$ females, 27 peaks total) and geriatric cycling ($n = 17$ females, 50 peaks in total) subjects. For noncycling females, we used maximal progestogen values attained as a comparison ($n = 4$ females).

Follicular Phase Lengths. We determined follicular phase lengths for each cycle of cycling females. We defined follicular phase values as points that remained beneath threshold and occurred between the end of 1 luteal phase and the onset of the next. We used follicular phase data to compare average follicular phase lengths between geriatric and control females

Average and Peak Progestogen Concentrations. Twenty-nine females remained for the analysis. We calculated overall mean progestogen values and mean luteal phase and follicular phase values for each female. We defined luteal phase values as all progestogen values that occurred from first sustained onset of threshold until sustained return to below threshold concentrations. We compared average luteal, follicular, and overall values for control females ($n = 8$), cycling geriatric females ($n = 17$), and noncycling females ($n = 4$). We did not include noncycling females in analyses of luteal phase length because sustained thresholds were absent. We used analysis of variance (ANOVA) to compare average progestogen values across the 3 sample groups. We defined peak progestogen value as the maximal progestogen value attained during a luteal phase. In this way, we calculated the average peak progestogen value for each luteal phase and averaged them for control ($n = 27$ peaks) and geriatric cycling ($n = 50$ peaks) females. For noncycling females, we used maximal progestogen value attained as a comparison. We then compared peak progestogen values across the 3 sample groups via ANOVA.

Behavioral Data Analyses

We compared the association between the occurrence of behavioral estrus with the onset of luteal phases, and evaluated proximity to a silverback. We included behavioral data for 16 of 22 geriatric and 4 of 8 control females. We collected behavioral data on average for 20 d/female over 3 mo. For each female, we identified episodes of sexual behavior and determined whether they occurred within luteal or follicular phases of the hormonal cycle. We compared the sexual episodes, which typically occurred within the follicular phase, with the timing of luteal phase onset. Then, to compare the relationship between behavioral estrus and onset of the luteal phase between geriatric and control females, we calculated the number of days between the first day marking the onset of successive days of estrous behavior and the first day marking the onset of the next luteal phase for each cycle/female. We calculated the average number of days between behavioral estrus and onset of luteal phase for each female and found the average for each group.

To evaluate whether distance from silverback is a measure of sexual behavior, we investigated whether females, for which we had behavioral data, spend more time in proximity to the silverback during presumed behavioral estrus than at other times. We collected data using 4 proximity categories: contact, < 1.5 m, 1.5–3 m, and >3 m. Because most females tended to remain >3 m from the silverback, we collapsed data into 2 categories: ≤ 3 m and >3 m, and calculated the percentage of time females spent in the distance categories when sexual behavior occurred vs. when sexual behavior was not apparent. We omitted females that never showed overt sexual behavior and those whose proximity to the silverback never exceeded 3% of total observation time, leaving 14 females for statistical analysis (sign test).

RESULTS

Hormonal Data Analyses

Baseline and Threshold Progestogen Concentrations

We calculated baseline progestogen and threshold values to be 195 ± 2.27 ng of progestogen/g of feces, and 292 ng of progestogen/g of feces, respectively. Final baseline and threshold values for the geriatric female whose baseline progestogen concentrations were higher than the others were 299 ± 15.9 ng of progestogen/g of feces and 450 ng of progestogen/g of feces, respectively, while the values for the control female whose baseline

progestogen concentrations were higher than the others were 320 ± 9.74 ng of progestogen/g of feces and 480 ng of progestogen/g of feces.

Cycle Lengths

While all 8 of the control females were cycling, with clear onsets of luteal phases, a number of geriatric females—5 of 22, or 22.7% of the sample—are no longer exhibiting regular hormonal cycles (Table I). The average age of cycling females is 39 ± 4.33 yr. Noncycling females are ≥38 yr, with an average age of 44 ± 5.03 yr. Among noncycling females, the most geriatric subject of the sample is, at 51 yr, among the oldest female gorillas in captivity. Noncycling geriatric females had irregular hormonal profiles; consequently, we could not use threshold values to determine cycle and follicular phase lengths (Fig. 1).

Estrus Cycle Length. We calculated estrus cycle lengths for the 25 cycling females, each with 1–4 cycles. Values for the average estrus cycle length in control (30.2 ± 2, range = 22–43, $n = 17$ cycles; mean ± SE) and geriatric cycling females (30.6 ± 2.1, range = 16–62, $n = 35$ cycles) are similar, but the 2 sample groups differed significantly in their variability ($F_{33,16} = 2.2, p < .05$).

Follicular Phase Lengths. We calculated values for average follicular phase lengths for control females (18.14 ± 1.7, range = 4–37), and geriatric females (19.7 ± 1.5, range = 4–56). Average values and variances between control and geriatric subjects do not differ statistically ($t = 1.2, p = .2$; $F_{36,21} = 1.7, p = .1$). CVs for the sample groups, 42% for control females, and 48% for geriatric females, further support that variability in the 2 samples is comparable.

Luteal Phase Lengths. We calculated values for average luteal phase lengths for control (11.2 ± .8, range = 4–19), and geriatric (9.7 ± 0.6, range = 2–17) Females. Average values and variances between control and geriatric subjects do not differ statistically ($t = -1.5, p = .1$; $F_{45,23} = .75$, $p = .2$).

Average and Peak Progestogen Concentrations

We found significant differences in overall progestogen concentrations among geriatric cyclers ($n = 17$), control females ($n = 8$), and geriatric noncycling females ($n = 4$; $F_{2,26} = 3.58, p = .04$). Average progestogen for geriatric noncyclers is 181.26 ± 26.6 (mean ± SE), while geriatric cycling females had an average of 286 ± 26.7, and control females averaged at 354.42 ± 39.72. Comparison of the means indicated that the statistical

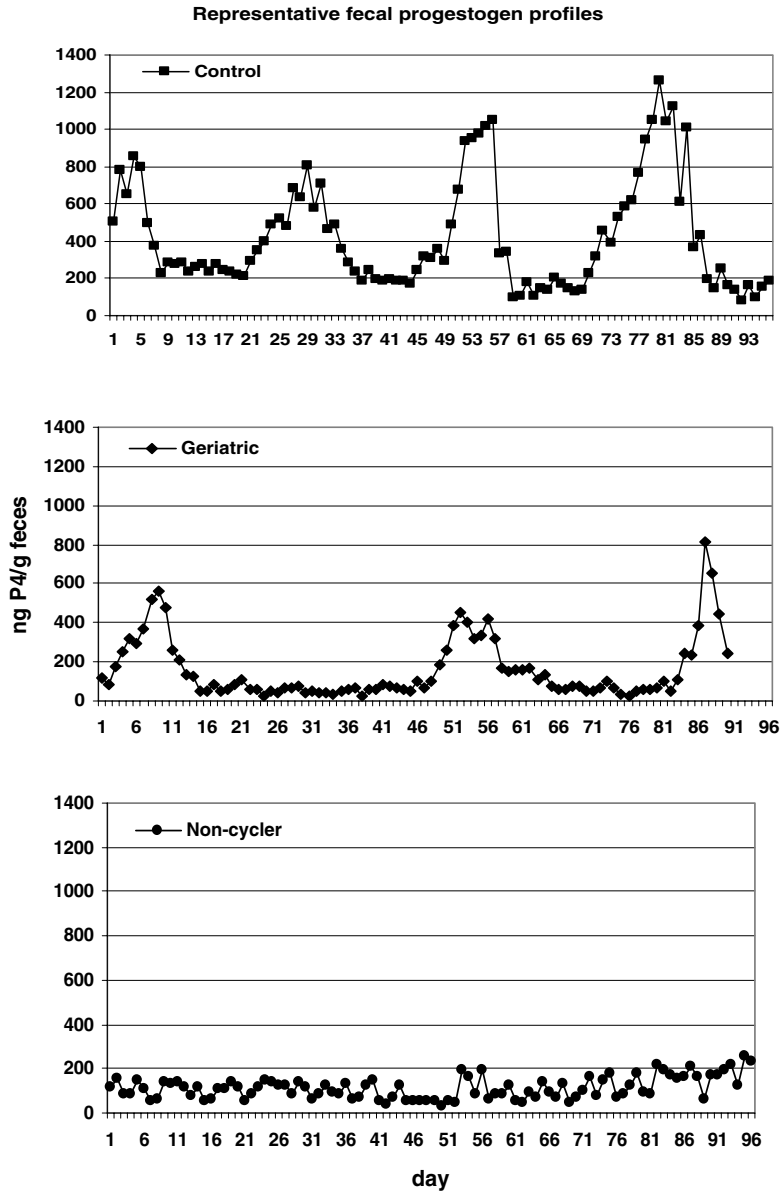

Fig. 1. Representative fecal progestogen profiles for a control female (*top*), a geriatric cycling female (*middle*), and a noncycling geriatric female (*bottom*). Note the difference in both the regularity and height of peaks for the geriatric vs. control female. The noncycling female does not exhibit any clear cyclical pattern, nor do progestogen values ever exceed threshold.

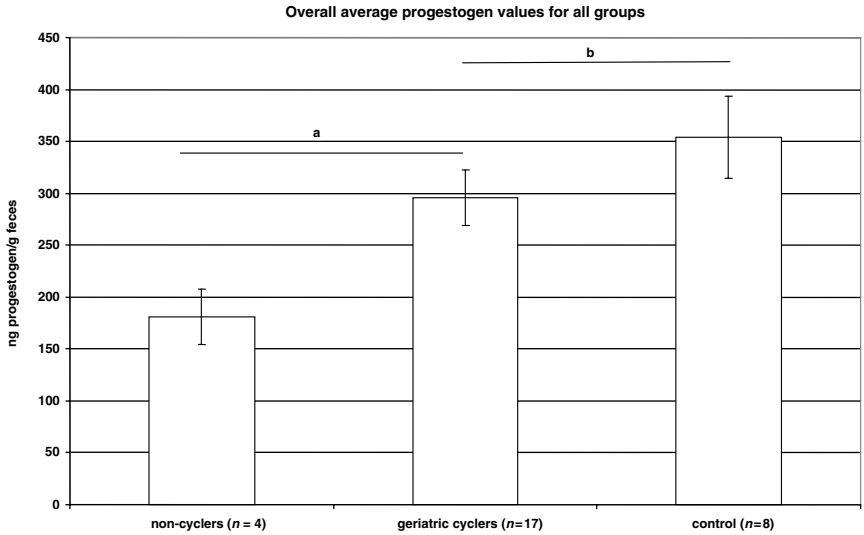

Fig. 2. Average (±SE) progestogen values for control, geriatric, and noncycling females. Lines indicate groups that are not significantly different from one another (Duncan's multiple-range test).

differences among the 3 groups of females are driven by the difference between control and noncycling geriatric females (Duncan's multiple range test, $p < .05$).

Peak progestogen concentrations are significantly lower for noncycling females than for cycling females, geriatric and control combined (ANOVA $F_{2,26} = 5.76$, $p = .01$). Noncyclers had an average peak level of 366.25 ± 38.9. Geriatric cycling females had an average peak value of 877.72 ± 74.6 and control females, 950.53 ± 116.5 (Fig. 2).

There is no significant difference between average luteal phase progestogen values in geriatric cycling females (553 ± 32.86) and control females (600.9 ± 41.4; $F_{1,21} = .74$, $p = .4$) or among average follicular phase progestogen values in geriatric cyclers (164.2 ± 12.4), control females (187.97 ± 23.2), and noncycling females (181.26 ± 26.6; $F_{2,24} = .98$, $p = .4$). In both cases, control females had higher average progestogen concentrations than those of geriatric females.

Geriatric Female Cycle Variability. For 7 of the cycling geriatric females we noted variability in maximum progestogen luteal phase values within their individual hormonal profiles. In the cycles of 2 females, luteal phase progestogen concentrations reached threshold values yet were considerably lower than progestogen concentrations in the remaining luteal phase

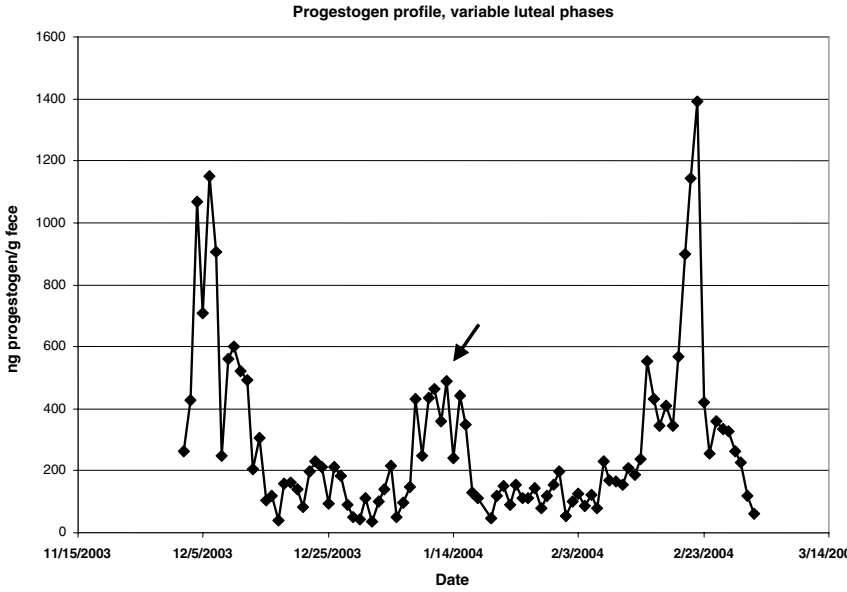

Fig. 3. Progestogen profile for a female that exhibited luteal phases with variable peak heights. Note the lower luteal phase, indicated by the arrow.

cycles (Fig. 3). In 3 other females, incipient progestogen increases, possibly indicating insufficient luteal phases, never reached or sustained threshold concentrations. That the low progestogen increases are luteal is supported in the case of 1 female that always cycled regularly both hormonally and sexually. In her case, even the low progestogen increase was preceded by estrous behavior, suggesting that the former was indeed luteal in nature. Variability was also obvious in the follicular phase lengths of 2 females in which extreme differences in number of days between luteal phases were apparent, suggesting that luteal phase increases are missing.

Behavioral Data Analyses

In the majority of females that displayed both physiological cyclicity and obvious sexual behavior there was an unmistakable relationship between signs of sexual behavior and hormonal cycles. Of the 4 control females for which we collected behavioral data, 3 showed detectable signs of estrous behavior, with an average of 4.3 d between first signs of behavioral estrus and onset of the next luteal phase ($n = 8$ cycle lengths, range

1–14 d). The control female that did not exhibit detectable estrus toward the male in her social group did, nevertheless, display sexual interest in the silverback housed adjacent to her. Of the 16 geriatric females on which we collected behavioral data, 3 were dual noncyclers, i.e., they exhibited neither hormonal nor sexual behavioral signs of cyclicity, and 1 exhibited behavioral signs but was not cycling hormonally. Two others exhibited signs that were not clearly associated with behavioral estrus. For the remaining 10 geriatrics, the average number of days between first signs of estrus and onset of next luteal phase was 6.6 ($n = 18$ cycle lengths, range 3–12 d), and was significantly longer than for control females ($t = 1.7$, $p \leq .05$, 1-tailed test). Of the 14 females for which we could assess proximity to silverback, 11 spent significantly more time in proximity to the male while also exhibiting behavioral estrus, as compared to nonestrus (sign test, $p < .05$).

DISCUSSION

Our study is the first attempt to quantify reproductive hormonal and associated behavioral patterns in a large sample of aging gorillas. Control females exhibited regular hormonal cycles but geriatric females showed a variety of patterns. Twenty-three percent of geriatric females in the sample are menopausal, characterized by complete lack of progestogen cycles. Thirty-two percent show indications of perimenopause; variability in either progestogen cycle lengths, magnitude of progestogen increases, or both suggests the occurrence of irregular ovulatory cycling. When comparing cycling geriatric with control females, we found differences in overall estrus cycle length, but not when comparing luteal and follicular phases independently. Similarly, we discovered higher overall concentrations of progestogen in control females than in geriatric females, but not when comparing luteal and follicular phase concentrations independently. The findings suggest trends toward increased variability in cycle length and lower progestogen concentrations in geriatric females that are revealed only when viewed across the entire cycle.

Seven of the cycling geriatric females had unusual patterns that we cannot fully interpret without additional hormonal data. Their hormonal profiles contained 1 cycle that was several-fold higher than the remaining ones. Extremely dry fecal samples can lead to uneven hormone increases, which may explain the observed pattern in 1 female. In the others, the elevated hormonal concentrations may reflect true intraindividual variation because values reach variability beyond what is typical of extraction and assay procedures (Bellem, Chicago Zoological Society endocrinology lab manager, *pers. commun.*).

Behaviorally, more than three-fourths of the females demonstrated estrus. Displays of proceptive behaviors, even anecdotal observations of sexual behavior, are closely associated with hormonal cycling; behaviors preceded the onset of cyclical progestogen increases, clearly occurring during the follicular phase. Intervals between sexual behavior and progestogen increases were longer for geriatric than for control females. Lastly, females spent more time in proximity to silverbacks when exhibiting behavioral estrus than at other times, suggesting that even in the absence of hormonal data a change in proximity may constitute a measure of sexual behavior that could signal the onset of estrus, even if other proceptive behaviors are absent. Thus, proximity may be an indicator of estrus because of its temporal correlation to behavioral estrus. The specific nature of sexual behavior among geriatric and control females varied and, we are currently analyzing the data.

Researchers have stated that reproductive cessation in nonhuman primates occurs close to the end of life (Austad, 1997). Indeed, macaques, which are, after humans, the most frequently researched primates, exemplify that reproductive failure is quite common in aging individuals (Small, 1984). However, reproductive cessation in primates does not occur abruptly but instead is preceded by age-related declines in fertility common to other mammals (Austad, 1997; Strum and Western, 1982). As in our study, age-related reproductive changes are variable. For example, even though female chimpanzees ≥33 yr old can become pregnant in the last year of their lives (Caro *et al.*, 1995), and have menstrual cycles until death (Fritz *et al.*, 2005), they also experience increased cycle lengths as they age (Fritz *et al.*, 2005; Graham, 1979). In some individuals, estrous swellings cease completely several years before death (Takahata *et al.*, 1995). In humans, too, declines in fertility associated with hormonal changes can occur as many as 20 yr before complete cessation of menstruation during the perimenopausal period. Nearly 30 yr ago Hodgen *et al.* (1977) claimed the existence of a perimenopause in nonhuman primates. Accumulating research has supported them (Black and Lane, 2002; Downs and Urbanski, 2004; Erwin *et al.*, 2002; Gilardi *et al.*, 1997; Gould *et al.*, 1981; Graham, 1979; Hodgen *et al.*, 1977; Jensen *et al.*, 1982; Johnson and Kapsalis, 1998; Martin *et al.*, 2003; Nozaki *et al.*, 1995; Shideler *et al.*, 2001; van Wagenen, 1972; Walker, 1995; Weiss, 2001). In humans the perimenopause is characterized by increasingly variable cycle lengths, shorter follicular phases, longer luteal phases, and declines in both estradiol and progestogens (Dudley *et al.*, 1998; Santoro *et al.*, 1996; vom Saal and Finch, 1988), the latter decreasing substantially in the 6 yr before menopause (Rannevik *et al.*, 1995). We found that aging gorillas that are still cycling experience patterns similar to those in human and other primate females: variability in cycle lengths in some

geriatric individuals, declines in overall progestogen concentrations, and occasional insufficient progestogen luteal phase increases. In noncycling gorillas we found substantial declines in progestogen concentrations, so low that in some cases values rarely exceeded the threshold values for cycling females, particularly in the control group. Noncycling females can be compared to humans in whom failure to exhibit luteal phase progestogen increases is a noticeable feature of the menopause (Burger *et al.*, 2002).

Though most of the aged females in our study were cycling, the question remains whether they can successfully reproduce. Information reported by the Species Survival Plan® for western gorillas indicates that fertility declines with age and that age-specific fecundity drops to near 0 at age >37 yr (Wharton and Thompson, 2000). Gorilla females in their mid-30s have reduced pregnancy rates and poor survival of offspring (Thompson, *pers. commun.*; Wharton, *pers. commun.*), possibly the result of less regular ovarian cycles (Lasley *et al.*, 1982; this study). In general, the findings parallel those for other primates, including humans. Japanese macaque and chimpanzee females may continue to ovulate, show estrus, and copulate for years after last parturition (Takahata *et al.*, 1995), some maintaining regular menstrual cycles despite decreased fertility and the approach of reproductive senescence (Nozaki *et al.*, 1995). Humans undergo dramatic fertility declines past their mid-30s despite continued menstrual cycling (Brenner *et al.*, 2004), with childbearing terminating up to a decade before menopause (Black and Lane, 2002). Pregnancy at an advanced age occurs in female gorillas; a 38-yr-old female recently gave birth at Zoo Atlanta in 2003 (Olson, *pers. commun.*), whereas the oldest female to have given birth was 42 yr old. However, based on a maximum lifespan of ≥52 yr for female gorillas in North American zoos, potentially up to 25% of their lives can be postreproductive, the same postreproductive span estimated for female chimpanzees (Nishida *et al.*, 1990, 2003).

Captive gorillas display a great deal of variability in reproductive success; single pregnancies early in life are not uncommon. Other females continue to breed regularly. Whether such differences are the result of social or physiological factors is unclear (Watts, 1991), and we were therefore concerned that the results of our study and the reproductive profiles of the subject females might reflect the state of primate husbandry rather than true gorilla reproductive patterns. But individual conditions of husbandry, health, and reproductive issues cannot account for the geriatric patterns because similar variability did not characterize the control group, suggesting that age is the primary factor behind the hormone profiles of the older subjects. Nevertheless, one must consider subject health during data collection. To illustrate, 1 control subject displayed demonstrably lower hormonal values than the other females in her group, even though she

appeared to be cycling normally. During an illness the following year, progestogen concentrations flatlined, suggesting that impending illness may have influenced low hormone values.

The noninvasive nature of fecal hormone analysis opens a range of research opportunities. As with any hormone monitoring technique, it is dependent on regular sample collection. Sometimes, even short gaps of 2–3 d, particularly in geriatric individuals, can obscure luteal phase increases that can be of relatively short duration. Of the female reproductive hormones, fecal analysis is restricted to estrogens and progestogens, somewhat limiting the information that can be gleaned because progestogen cycles, even with associated displays of estrus, are not always ovulatory (Mitsunaga *et al*., 1992). Though concentrations of basal progestogens can provide information on hormonal cycling, FSH and luteinizing hormone (LH) levels, obtained via serum or urine analysis, can reveal menopausal transition (Hodgen *et al.*, 1977). Therefore, in the sample, we consider that the females lacking progestogen cycles are anovulatory and consequently in menopause, but whether or not the cycling geriatric females are ovulating is less obvious. Even so, given the advantages of using fecal samples to monitor hormones, and the potential to examine hormonal cycling in wild primate populations, use of the technique may lead to detailed information on cyclicity and reproductive aging in the future.

Though reproductive output may end at a particular age, advances in veterinary care and improved nutrition of captive primate populations have extended average longevity far beyond the age typical of reproductive termination. Primate gerontologists have flagged the importance of older individuals to understand the aging process because, through noninvasive long-term age-related studies, captive populations can contribute to comparative analyses between humans and other primates (DeRousseau, 1994; Erwin *et al.*, 2002; Martin *et al.*, 2003). Zoological institutions are vital to such studies, especially because age and general history data are readily available. With sample sizes that are unparalleled for apes and other species in the wild, zoos can figure prominently in endeavors to understand longevity, physiology, life history, and aging (DeRousseau, 1994).

Captive conditions may be artificial but the relative uniformity that they provide across institutions and species ensures that variation in longevity is likely to reflect differences in genetic potential (DeRousseau, 1994). If improved care is helping captive populations to reach species-specific potential for longevity, then the genetic potential of gorillas exceeds 50 yr. Our results attest to measurable age-related changes in aging female gorillas, clearly documenting perimenopausal and menopausal conditions. Given the extended longevity of female gorillas, continued longitudinal monitoring of their reproductive physiology and behavior is now

clearly warranted. Not only will additional research provide valuable insights into the care and management needs of geriatric gorilla females, but it will also help to develop a comparative model for human reproductive aging with respect to both menopausal and, perhaps more importantly, perimenopausal changes.

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