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Aging in the Natural World: Comparative Data Reveal Similar Mortality Patterns Across Primates

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Human senescence patterns—late onset of mortality increase, slow mortality acceleration, and exceptional longevity—are often described as unique in the animal world. Using an individual-based data set from longitudinal studies of wild populations of seven primate species, we show that contrary to assumptions of human uniqueness, human senescence falls within the primate continuum of aging; the tendency for males to have shorter life spans and higher age-specific mortality than females throughout much of adulthood is a common feature in many, but not all, primates; and the aging profiles of primate species do not reflect phylogenetic position. These findings suggest that mortality patterns in primates are shaped by local selective forces rather than phylogenetic history.

Humans are thought to age more slowly than other mammalian taxa [(*1*), but see (*2*)] on the basis of their low early-adult mortality, slow mortality acceleration, and long life span. However, it is not known if these human features are unique or are shared with other primates (*3*, *4*). The rapid increase in human life expectancy in the 20th century (*5*) has increased the proportion of individuals in older age classes (*6*), raising questions about the flexibility of human aging patterns and the limits of the human life span [e.g., (*7*–*9*)]. These questions necessitate a deeper understanding of natural aging patterns in other primates, which represent our closest living relatives (*10*).

Nonhuman primates, like humans, are cognitively and socially complex and behaviorally flexible. However, their long lives and the challenges of continuous, long-term observation make longitudinal demographic data on nonhuman primates uncommon, especially for wild populations [(*11*); see also (*12*)]. We compiled rare data sets from seven species that span the Primate Order [one Indriid (a Madagascan prosimian), two New World monkeys, two Old World monkeys, and two great apes] and carried out a comparative demographic analysis of mortality. Our analyses used data from 226 observation-years of births and deaths on more than 2800 individually recognized male and female primates (*13*, *14*).

We produced species-specific mortality tables for each sex and computed actuarial estimates of age-specific survival and mortality for each of

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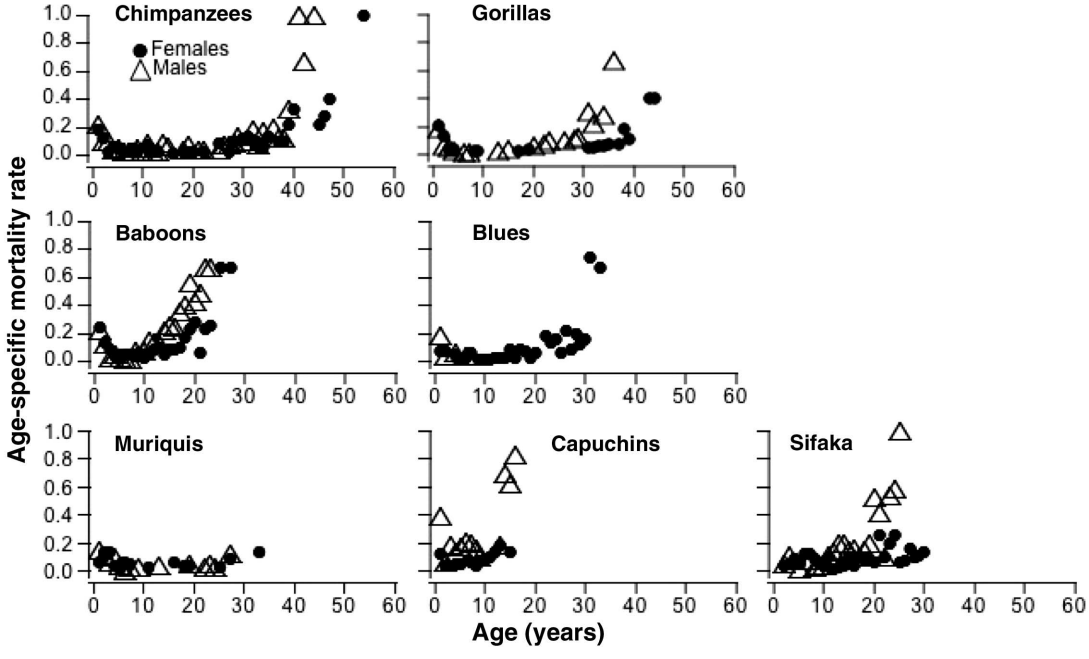


Fig. 1. Age-specific mortality at age x, u_x, for each study species, illustrating high infant mortality, low juvenile mortality, and mortality increasing with age over the adult life span. No sex-specific first-year mortality estimates are available for sifaka because individuals were not sexed and individually identified until their first birthday. For blue monkey males and both sexes of capuchins and muriquis, mortality estimates extend only through age 6, 20, and 32 years, respectively; in each case, this is much less than the suspected full life span, making it difficult to estimate the shape of the mortality curve at the end of life.

the primate populations (*15*). Analysis of mortality rates revealed the expected pattern for mammals: high infant mortality, followed by a period of low mortality during the juvenile stage, and an extended period of increasing age-specific mortality during mid to late life (Fig. 1). We focused on mid- to late-life demography and modeled initial mortality rate at the start of adulthood for each species, defined in Table 1, through the last age interval for which we had census data. For humans, we used published male and female age-at-death data, from age 15 through 100 years, from the U.S. Department of Health and Human Services life tables (*16*) and repeated the analyses with a second, independent life table for humans (*17*), which confirmed our findings.

Understanding flexibility and constraints in the expression and evolution of aging requires a careful analysis of key aging metrics (*1*, *18*, *19*). We used a maximum-likelihood framework for estimating two metrics that, together, describe the pattern of senescence for a population: the initial adult mortality rate (*IMR*, the risk of death at onset of adulthood) and the rate of aging (*RoA*, the rate of increase in the age-specific mortalities with advancing adult age). These aging metrics are often best estimated by fitting the Gompertz model of increasing failure time. We thus tested among competing models for accelerating risk of death with advancing age on the basis of the Gompertz family of models in program WinModest (*20*) model fitting as described in (*21*). Our tests included a standard two-parameter Gompertz model and the Gompertz-Makeham and Logistic models. In all but 2 of the 13 species and sex comparisons we examined, the standard two-parameter Gompertz model yielded the best fit to the nonhuman primate data. In the other two cases (sifaka females and capuchin males), the Gompertz-Makeham model was recommended, but because of particular features of those two data sets (see table S1), we proceeded with the standard Gompertz model for males and females of all species. Our model was of the form $u_x = IMR \times e^{(RoA)x}$, where u_x is the age-specific mortality, i.e., instantaneous mortality probability, at age x (results in Tables 2 and 3 for females and males, respectively).

We found significantly positive values for *RoA* in all study species, indicating that mortality rate increased with advancing age [Tables 2 and 3 and fig. S1; see also (*22*, *23*)]. Notably, humans fell along a continuum with the other primate species for both *IMR* and *RoA* (Fig. 2). Furthermore, in neither females nor males did we find evidence of a negative correlation between *IMR* and *RoA*, which would be indicative of a trade-off between these two parameters (Fig. 2). Instead, our data suggest that they can evolve independently. Humans had low values for both parameters, which explains their exceptional longevity.

For females, we identified four distinct groups of *IMR* across the eight species (Fig. 2A). All species comparisons were computed on the basis of χ^2 tests of pairwise comparisons of the log-likelihood ratio of models with unique versus identical Gompertz parameters (table S2). We identified three significant groups for *RoA* (Fig. 2A). The coefficient of variation among species for female *IMR* was 111%, much greater than that for *RoA*, which was 30%; females of these primate species exhibited a wide range of *IMR* values,

Table 1. Summary of study populations. Details about and references for study sites are in (*15*).

Common name	Species	Family	Country	Avg. annual rainfall (mm)*	Life-style	Start year †	Sample size		Adult age‡		Predominant dispersing sex	Mean age of first dispersal (years)
							M	F	M	F		
Sifaka	*Propithecus verreauxi*	Indriidae	Madagascar	578	Arboreal	1984	291	219	5–6	6–7	M	4–5
Northern Muriqui	*Brachyteles hypoxanthus*	Atelidae	Brazil	1180	Arboreal	1983	192	212	6–7	8–9	F	6–7
Capuchin	*Cebus capucinus*	Cebidae	Costa Rica	1736	Arboreal	1983	98	58	6–7	6–7	M¶	4–5
Yellow baboon	*Papio cynocephalus*	Cercopithecidae	Kenya	347	Semi-terrestrial	1971	489	437	7–8	5–6	M	7–8
Blue monkey	*Cercopithecus mitis*	Cercopithecidae	Kenya	1962	Arboreal	1979	128	194	8–9	7–8	M	7–8
Chimpanzee	*Pan troglodytes*	Hominidae	Tanzania	1330	Semi-terrestrial	1963	122	144	14–15	14–15	F	12–13
Gorilla	*Gorilla beringei*	Hominidae	Rwanda	1358	Terrestrial	1967	128	120	15–16	9–10	M#	15–16
											F	7–8

*Average annual rainfall for each study, representative of the study years. Rainfall data for gorillas were collected by the Rwandan Government Meteorological Office at a location several kilometers from the field site and at a lower elevation. Rainfall data for other studies were collected at the study site. †Year study was established. Latest census date for all populations in these analyses was December 2008. ‡Mean age class at which adulthood is attained for each sex. Male onset of adult stage was defined as mean age of likely first reproduction (using physical criteria such as copulation with ejaculation, behavioral criteria such as the onset of mate guarding behavior, or genetically confirmed paternity). Female onset of adult stage is defined as the mean age of first live birth. ¶Twelve percent of female capuchins disperse. The average age interval of dispersing capuchin females is 6 to 7 years. #Both sexes disperse in gorillas.

Table 2. Gompertz estimates of female mortality parameters and life-span summary statistics. Adult age interval is the age interval containing the mean age of first live birth; *IMR* (= Gompertz *a*) is the Gompertz estimate of instantaneous mortality rate at the first adult age interval [with its 95% confidence interval (CI)]; *RoA* (= Gompertz *b*) is the adult rate of aging estimated with Gompertz acceleration (with its 95% CI); MRDT is the mortality rate doubling time during adulthood; Oldest age reached is the age class of the oldest observed individual; Median age is the 50% survival age with its range.

Species	Adult age interval (years)	*IMR* (/year)	95% CI	*RoA*	95% CI	MRDT (no. of years)	Oldest age reached (years)		Median age	[Range]
							Estimated	Known*		
Sifaka	6–7	0.0278	[0.019, 0.0410]	0.0991	[0.072, 0.136]	7.0	31–32	23–24	10	[9, 12]
Muriqui	8–9	0.00170	[0.00042, 0.00685]	0.129	[0.0722, 0.230]	5.4	40–41	26–27	25	[18, 33]
Capuchin	6–7	0.0415	[0.0150, 0.114]	0.165	[0.055, 0.494]	4.2	26–27	19–20†	11	[10, 13]
Baboon	5–6	0.0285	[0.020, 0.040]	0.123	[0.0926, 0.165]	5.6	27–28	27–28	8	[7, 9]
Blue monkey	7–8	0.00723	[0.00367, 0.0143]	0.160	[0.123, 0.209]	4.3	33–34	26–27	18	[17, 22]
Chimpanzee	14–15	0.00774	[0.0038, 0.0156]	0.0992	[0.070, 0.140]	7.0	53–54	38–39	16	[10, 25]
Gorilla	9–10	0.00028	[0.00004, 0.00214]	0.211	[0.148, 0.300]	3.3	43–44	38–39	33	[31, 35]
Human‡		0.00009	[0.00008, 0.00009]	0.0961	[0.0956, 0.0967]	7.2	100+	100+	83.5	

*Oldest individual with known date of birth. †Truncated at 18–19 for mortality analysis because of relatively smaller sample sizes of deaths and transitions in later age classes. ‡Data from (*16*), modeled beginning at age interval 15–16 years through 99–100 years.

whereas *RoA* was less variable (equality of variance test: $F_{7,7} = 6.44$, $P = 0.02$). Moreover, all combinations of high and low *IMR* with high and low *RoA* were found in the females of the seven nonhuman species. For example, female chimpanzees were characterized by both low *IMR* and low *RoA*, whereas female sifaka exhibited high *IMR* but relatively low *RoA*. In contrast, female gorillas had low *IMR* and high *RoA*, while female capuchins exhibited both high *IMR* and high *RoA*. The *RoA* for human females was statistically indistinguishable from that of the four other slowly aging female primates (Fig. 2A and table S2). Human females had one of the two lowest *IMR*s (statistically indistinguishable from gorilla; Fig. 2A and table S2), but this trait is arguably more reflective of environmental plasticity than is *RoA* (*24*). This similarity between humans and nonhuman primates indicates that aging in humans is not evolutionarily divergent from that in other primate species [see also (*1*)]. This similarity is particularly noteworthy given that our human-nonhuman comparison was a conservative one, in that it used data from modern human populations rather than hunter-foragers or historical populations [which might resemble wild nonhuman primates more than modern humans do (*23*, *25*)].

Among males, the coefficient of variation for *IMR* was 107%, much greater than the coefficient of variation in *RoA*, which was 40% (equality of variance $F_{6,6} = 26.0$, $P = 0.001$). Males and females showed similar variation in *IMR*, but males showed greater variation than females in *RoA*. Males exhibited fewer combinations of *IMR* and *RoA* than females: Baboon, sifaka, and capuchin males were characterized by high *IMR* and high *RoA*, whereas gorilla, muriqui, and chimpanzee males had intermediate *IMR* and intermediate *RoA*. Like females, males exhibited four significant groupings of *IMR* and three significant groupings of *RoA* (Fig. 2B and table S2). *RoA* in human males, unlike in human females, was significantly lower than the next closest value, that of chimpanzees, and the *IMR* for human males was relatively even lower (Fig. 2B).

Males of monogamous animal species tend to age at rates similar to those of females, whereas males of polygynous species exhibit increased aging rates relative to females (*26*, *27*). All of the nonhuman primate species studied here are polygynous (or more accurately polygynandrous, as multiple mating is exhibited by females as well as males). Further, six of the seven experience relatively intense male-male competition for access to mates [see (*28*) for genus-level data on *Cebus*, *Cercopithecus*, *Gorilla*, *Papio*, and *Pan*; (*29*) for data on *Propithecus*]. The exception is the muriqui, a sexually monomorphic species in which male-male competition for access to females appears to be absent (*30*). In the species with relatively

Table 3. Gompertz estimates of male mortality and life-span summary statistics. Adult age interval is the mean age class of likely first reproduction. *IMR* (= Gompertz *a*) is the instantaneous mortality at adulthood (with its 95%CI); *RoA* (= Gompertz *b*) is the rate of aging estimated with Gompertz acceleration (with its 95% CI); MRDT is the mortality rate doubling time during adulthood; Oldest age reached is the age class of the oldest observed individual; Median age is the 50% survival age with its range.

Species	Adult age interval (years)	*IMR* (/year)	95% CI	*RoA*	95% CI	MRDT (no. of years)	Oldest age reached (years)		Median age	[Range]
							Estimated	Known*		
†Sifaka	5–6	0.0201	[0.0140 0.0290]	0.186	[0.155, 0.222]	3.73	26–27	19–20	12	[12, 13]
Muriqui	6–7	0.00187	[0.00044, 0.00784]	0.148	[0.0820, 0.266]	4.70	33–34	26–27	24	[22, 27]
Capuchin†‡	6–7	0.010	[0.0027, 0.036]	0.294	[0.159, 0.542]	2.36	24–25¶	12–13	4	[3, 5]
Baboon†‡	7–8	0.0371	[0.0266, 0.0517]	0.213	[0.177, 0.256]	3.26	24–25	22–23	10	[9, 11]
Blue monkey	8–9	No est.		No est.			19–20	19–20	No est.	
Chimpanzee	14–15	0.00787	[0.00346, 0.0179]	0.137	[0.0980, 0.190]	5.07	43–44	40–41	11	[9, 14]
Gorilla	15–16	0.00594	[0.00139, 0.0254]	0.182	[0.106, 0.313]	3.81	38–39	34–35	23	[22, 29]
Human‖		0.00024	[0.00023, 0.00025]	0.086	[0.0854, 0.0863]	8.07	100+	100+	79.5	

*Oldest individual with known date of birth. †Distribution of deaths imputed from onset of adulthood with age structure. See methods in the Supporting Online Material (SOM). ‡Age structure corrected for population growth. See methods in the SOM. ¶Truncated at 18–19 for mortality analysis because of relatively smaller samples sizes of deaths and transitions in later age classes. ‖Data from (*16*), modeled beginning at age interval 15–16 years through 99–100 years.

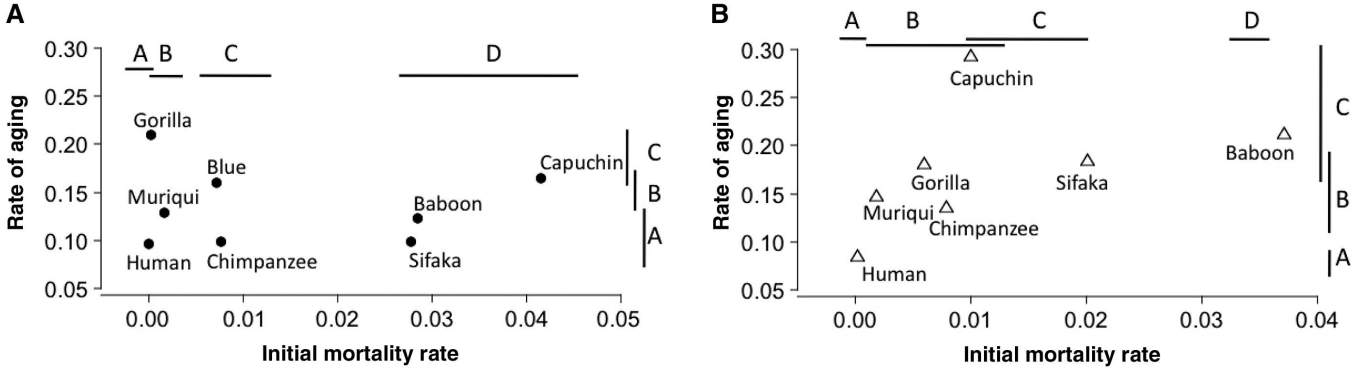
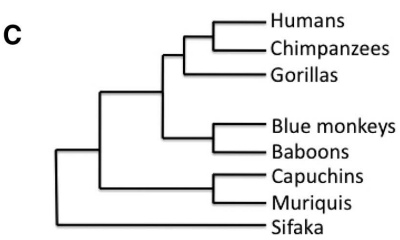


Fig. 2. *IMR* versus *RoA* for (**A**) females and (**B**) males. Phylogenetic relationships among species are shown in (**C**). Letters over bars denote statistically significant groupings. [Female *IMR*: human, gorilla (A) ≤ gorilla, muriqui (B) < blue monkey, chimpanzee (C) < sifaka, baboon, capuchin (D); female *RoA*: human, chimpanzee, sifaka, baboon, muriqui (A) ≤ muriqui, blue monkey, capuchin (B) ≤ blue monkey, capuchin, gorilla (C); male *IMR*: human (A) < muriqui, gorilla, chimpanzee, capuchin (B) ≤ capuchin, sifaka (C) < baboon (D); male *RoA*: human (A) < chimpanzee, muriqui, gorilla, sifaka (B) ≤ muriqui, gorilla, sifaka, baboon, capuchin (C).] See table S2 for tests of pairwise comparisons of *IMR* and *RoA*.



intense male-male competition for mates, males and females showed significant differences in either *IMR* or *RoA*, and male life span was shorter than female life span (baboons, sifaka, gorillas, chimpanzees, and capuchins; we lacked mortality data for male blue monkeys; see Fig. 1 and table S3). In contrast, male and female muriquis were indistinguishable in their *IMR*s, *RoA*s, and life spans (table S3). This male-female similarity in muriqui aging patterns, combined with the observation of multiple mating by both sexes in all of our study species, suggests that the male-male competitive environment, not just multiple mating by males, may be a key factor driving faster aging in males in polygynandrous species [see also (*26*)].

If demographic patterns of aging were evolutionarily constrained, we would expect closely related species of primates to exhibit similar aging patterns. Instead, the species rankings of *IMR* and *RoA* in males and females showed no relationship to phylogeny (Fig. 2C and fig. S1). This implies that the study species have not been constrained phylogenetically to high or low aging rates, and have the flexibility to respond to evolutionary forces at the species level or potentially even the local population level. Furthermore, within-species comparisons of baboons (*31*), chimpanzees (*23*, *32*), and humans (*23*, *25*) all support the view that both *IMR* and *RoA* can vary substantially among populations within a species. Notably, in all three species, populations existing in more demanding habitats, without benefit of modern medical intervention (e.g., hunter-forager humans and wild as opposed to captive primates), exhibit higher *IMR* and, for both chimpanzees and humans, higher *RoA*. That is, aging appears to be both evolutionarily labile and phenotypically plastic. The slowing of aging-related disease under dietary restriction (*33*) is further evidence of the flexibility of aging rates in primates.

We examined our data for the existence of mortality plateaus (*34*), a subject of much recent interest in the aging literature, but none of the age-specific mortality relationships in our nonhuman primate analyses demonstrated the type of leveling off that has been shown in human and fly data sets [e.g., (*35*)]. Whether additional long-term data from natural primate populations will demonstrate a generalized mortality deceleration in old age remains an open question that should motivate future comparative analyses of aging in other natural populations.

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Supporting Online Material

www.sciencemag.org/cgi/content/full/331/6022/1325/DC1
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Positive Supercoiling of Mitotic DNA Drives Decatenation by Topoisomerase II in Eukaryotes

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DNA topoisomerase II completely removes DNA intertwining, or catenation, between sister chromatids before they are segregated during cell division. How this occurs throughout the genome is poorly understood. We demonstrate that in yeast, centromeric plasmids undergo a dramatic change in their topology as the cells pass through mitosis. This change is characterized by positive supercoiling of the DNA and requires mitotic spindles and the condensin factor Smc2. When mitotic positive supercoiling occurs on decatenated DNA, it is rapidly relaxed by topoisomerase II. However, when positive supercoiling takes place in catenated plasmid, topoisomerase II activity is directed toward decatenation of the molecules before relaxation. Thus, a topological change on DNA drives topoisomerase II to decatenate molecules during mitosis, potentially driving the full decatenation of the genome.

In eukaryotes, most topological links between the DNA strands are removed during DNA replication by topoisomerases I and II (fig. S1A) (*1*). However, many links are converted into double-stranded DNA intertwines or catenanes during the completion of replication (*2*, *3*). These can only be resolved by topoisomerase II (fig. S1) (*4*).

Passage through mitosis is required for complete decatenation, because topoisomerase II activity is essential during mitosis as late as anaphase (fig. S1B) (*4*–*6*). Because mitotic spindles are required to complete decatenation, it is assumed to occur only after chromosome segregation during anaphase (*4*). However, sister chromatids appear to be fully decatenated before their physical separation by spindles (*7*, *8*). Potential alternate mechanisms, in which decatenation is promoted by supercoiling, have been proposed in prokaryotes (*9*–*11*). These mechanisms prompted us to study whether mitotic changes to DNA topology help drive decatenation in eukaryotes.