Parental age at conception on mouse lemur's offspring longevity: Sex-specific maternal effects

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Abstract

Parental age at conception often influences offspring’s longevity, a phenomenon referred as the “Lansing effect” described in large variety of organisms. But, the majority of the results refer to the survival of juveniles, mainly explained by an inadequate parental care by the elderly parents, mostly the mothers. Studies on the effect of parental age on offspring’s longevity in adulthood remain few, except in humans for whom effects of parental age vary according to statistical models or socioeconomic environments. In a small primate in which the longevity reaches up to 13 years, we investigated the effects of parental age at conception on the longevity of offspring (N = 278) issued from parents with known longevity. None of the postnatal parameters (body mass at 30 and 60 days after birth, size and composition of the litter) influenced offspring’s longevity. Mothers’ age at conception negatively affected offspring’s longevity in males but not in females. By contrast, fathers’ age at conception did not influence offspring’s longevity. Finally, the longevity of female offspring was significantly positively related to the longevity of both parents. Compared with current studies, the surprisingly minor effect of fathers’ age was related to the high seasonal reproduction and the particular telomere biology of mouse lemurs.

Introduction

Longevity varies greatly among individuals and increasing evidence suggests that parental age affects longevity of offspring: the longevity of offspring of older parents is shorter than that of the offspring of younger parents. This phenomenon referred as the “Lansing effect” has been described in many taxa including more than 300 species [1, 2]. The underlying mechanisms mainly rely on the age-related changes of germ cells and particularly of telomeres [3, 4]. However, the majority of results confirming the “Lansing effect” refer to juveniles’ survival, which is mainly explained by an inadequate parental care of aged parents. Depending on the father’s role in parental care, sex differences exist for the effects of mothers’ age on juveniles’ survival. In birds, juveniles’ survival may be favored by older females, but it also largely depends on the resources provided by the father [5–9]. In fact, the influence of parent’s age can be reduced, even absent, when the environmental conditions are favorable.
In mammals, most of studies refer to the negative effects of mothers’ age on the pre-adult survival [2], whereas a few studies reported the role of the paternal age at conception on offspring survival [10, 11].

In humans, numerous recent studies have tested the “Lansing effect” on pre-industrial populations [10, 11] or on modern societies [12–14]. Despite extremely large samples (from 10,000 to more than five millions of people), contradictory results on the effects of parental age on the longevity of children were described, either negative or positive, depending on the statistical models, on the methods used or on the socio-economic environment to which the lengthening human longevity plays a preponderant role [15, 16].

Among non-human primates, studies on the effects of parental age on adult survival remain rare because of their great longevity and their low reproduction rate. By contrast, Malagasy prosimians constitute a more suitable model owing to their higher reproduction rate and their lower longevity. Among Malagasy species, juvenile survival until weaning is maximal when mothers are middle-aged but rapidly decreases reaching less than 20% for oldest females [17–19]. However, few studies investigated the relationship between parent’s age and longevity of offspring at adulthood.

To test the “Lansing effect”, we focused on the grey mouse lemur, a Malagasy primate. In captivity, although individuals who survived past 16 years have been recorded [20], its longevity may reach up to 13 years [21] with a median lifespan averaging 5.5 years [22]. Mouse lemurs are strict long-day photoperiodic breeders [23]. At the beginning of the breeding season, females enter oestrus and males compete to priority access to females [24]. Females give birth to 1 to 3 offspring after a 2-month gestation period and nurse infants for approximately 40 days without male parental care. Records of ages at conception for both mothers and fathers and the relative long longevity of captive mouse lemurs give the opportunity to test the “Lansing effect”.

Using a large database on captive mouse lemur’s life history traits, the aim of this study was to examine whether parental age at conception affects the longevity of offspring. We expected a reduced longevity of offspring born from old parents. Finally we tested the potential relationship between parents’ and offspring’s longevity.

**Material and methods**

**Animals**

To investigate the effects of parental age at conception on offspring lifespan, we analysed the longevity data of mouse lemurs for which the age of both parents at the time of reproduction was known. Data were recorded in the mouse lemur history traits database from a laboratory breeding colony established in Brunoy (UMR 7179 MNHN-CNRS, IBISA Platform, agreement F91.114.1, DDPP Essonne, France) from a stock originally caught near the southern western coast of Madagascar sixty years ago.

Captive conditions were maintained constant with respect to ambient temperature (24–26 °C) and hygrometry (55–60%). Animals were fed *ad libitum* on a standardized diet, including fresh fruits, a homemade milky mixture (19.3% proteins, 17.2% lipids and 63.5% carbohydrates) and mealworms. To ensure seasonal reproductive rhythms, animals were routinely exposed to an artificial photoperiodic cycle consisting of 6 months of summer-like photoperiod (LD = 14 h of light/day) followed by 6 months of winter-like photoperiod (SD = 10 h of light/day) [23]. The beginning of the breeding season was induced by the exposure to long days. At the time of LD exposure, groups of 2–3 unrelated males with 1 to 3 females were randomly constituted. Immediately, males entered competition for priority of access to oestrous females, leading to a hierarchy mostly depending on aggressive interactions [25]. During
sexual competition, several nest boxes were provided so that animals can escape agonistic
interactions from conspecifics and the chase or fight immediately stops when the chased ani-
mal enters a nest-box. In the colony, heterosexual groups were restricted to the few days of
female estruses. The rules set in the breeding colony for reproductive events included: the lim-
ited number of breeding by year, the female age, body mass of sexual partners, maternal line-
age and previous reproductive success. Paternity determinations, recorded in the database,
allowed calculating the reproductive success of each male within a group. After mating, males
were kept in single-sex groups, and females were isolated for gestation, birth and lactation. Lit-
ter size and composition were recorded at birth.

Data analysis
Our analysis was focused on parents (132 dams and 122 known sires) and their offspring (140
males and 138 females) that died naturally.

Paternity determinations have been previously determined by behavioural observations
and genetic analyses and were registered in the database. Briefly, DNA samples were collected
from ear or skin tissue samples, extracted (with a QIAmp DNA Mini Kit no. 51306—Qiagen)
and amplified. Genetic analyses were then conducted using random amplified polymorphic
DNA method or microsatellite loci [25–27].

To assess which parameters may influence the longevity of offspring, several parameters for
both parents and offspring were selected. Data are presented as mean± SEM.

First, age at conception for both parents was considered. dams’ age at conception averaged
2.7 ± 0.1 years (N = 278), the majority of dams being less than 5 years old; dams aged more
than 5 years old represented only 8%. Several dams have had several litters with different sires
(N = 19). Sires’ age at conception was significantly higher than that of dams (3.2 ± 0.1 years,
df1/554: F = 16.0, P < 0.001) and 85% of sires were less than 5 years old. Parents could have off-
spring from the first breeding season (minimum 260 days), and can reproduce until death like
to other prosimians species [18, 19, 28]. In our sample however, due to management reasons,
parental age at breeding did not exceed 8 years. In this study, parents were considered young
when ≤ 2 years old, adults when > 2 to 5 years old, and aged when > 5 years old. Second,
parents’ lifespan was included in the analyses.

For offspring, only young that were alive when 6 month-old were included in this study.
Dams’ parity was not included because previous studies demonstrated that this parameter did
not influence the size or the composition of the litters, or growth rate during the first month of
life [29]. However, size (from 1 to 3 offspring) and type of litter in which offspring were born:
male litters (M, MM, MMM), female litters (F, FF FFF) and mixed-sex litters (MF, MMF,
MFF) were considered.

Body mass (g) at 30 days, i.e. near weaning time (N = 267), thus providing a clue on mater-
nal investment, as well as at 2 months after birth (N = 273) were included. Age and timing
relative to the photoperiodic regimen of natural death were incorporated in the analyses.
Lastly, because of the energy costs of mating [30] opportunities for offspring to mate, were also
recorded.

Statistics
Data are presented as means ± SEM. Statistical analyses included Cox proportional hazards
model, multi-way analyses of variance using or not a covariate and G tests to test distributions.
Multiple pairwise comparisons were made using Tukey’s post hoc test. Relationships between
the different factors were tested using linear regression analyses. All statistical analyses were
conducted using Systat Software.
Ethics statement

All the results in this study did not correspond to experimental procedures but are issued from the exploitation of lifespan data collected in the long-term mouse lemur’s captive population maintained for scientific purposes. We adhered to the Guidelines for the Treatment of Animals in Behavioural Research and Teaching [31] and the legal requirements of the country (France) in which the work was conducted. The colony is established under the authorisation of the Direction Départementale de Protection des Populations (DDPP/022-F91-114-1). All procedures to breed mouse lemurs are conducted in accordance with the European Communities Council Directive (86/609/EEC) and are authorized by the Departmental Veterinary Services (Directive 2010/63/UE—Capacity certificate Préfecture de l’Essonne, 04/03/1995). Specifically, for these arboreal primates, housing conditions include cages equipped with branches, various supports, devices to stimulate foraging, and many nesting boxes allowing the animals to express their entire behavioural repertoire. The health and the well-being of captive animals are regularly checked by the animal care keepers and the veterinarian. To improve animal welfare and the enrichment of breeding conditions, meetings of the welfare unit are held every month. When an animal shows signs of poor conditions or signs of social distress, it is isolated and monitored until fully recovered. Lastly, only animals that were found dead were used to conduct longevity research, so effects of anaesthesia, euthanasia or animal sacrifice influenced this study.

Results

1) Offspring longevity and postnatal parameters

Using Cox proportional hazards model, the median lifespan of offspring examined in this study reached 5.5 ± 0.1 years (N = 278) without a significant difference between males (5.53 ± 0.2 years, N = 140) and females (5.46 ± 0.2 years, N = 138, df1/276, F = 0.12, P > 0.7). Maximal lifespan reached 12.1 years in males and 11.1 years in females. Natural deaths mainly occurred at the photoperiodic transitions (43%, Gdf2 = 13.6, P < 0.010) but were significantly more frequent during long-day photoperiod (df1/274, F = 4.96, P = 0.024) independently of sex (df1/274, F = 0.01, P > 0.9).

Size and type of the litter. Offspring mainly issued from litters of 3 (55%), with litter size of 1 or 2 representing 9% and 36% respectively; the distribution of litter size was identical within sexes (Gdf2 = 2.13 P > 0.3). Mixed sex litters were most prevalent (63%) among offspring studied.

Dams’ age at conception had an impact on the size of the litter produced (r = 0.159, P = 0.008), with young dams producing less numerous triplets than older dams (45% versus 66% respectively—df2/275, F = 3.25.18, P = 0.039). The type of the litter was independent of the dam’s age (df2/275, F = 0.002, P > 0.9). By contrast, whereas sires’ age had no impact on litter size (r = 0.092, P > 0.1), younger sires produced less numerous male-biased litters (df2/275, F = 4.3, P = 0.015).

Accordingly, the size and the type of the litter were dependent on both parents with adult pairs producing more numerous offspring (63%) in more numerous male-biased triplets (litter size df2/275, F = 4.09, P = 0.022 and litter type df2/275, F = 5.99, P = 0.003).

But offspring longevity was independent of the size (df2/275, F = 0.73, P = 0.5) and of the type of the litter (df2/274, F = 0.08, P > 0.7), whatever the offspring sex (df2/274, F = 0.08, P > 0.9—Fig 1).

Post natal body mass. Offspring body mass reached prior to weaning time (30 days) averaged 32.1 ± 0.4g (N = 266—Table 1). It was independent of both dams’ age (r = 0.043, P > 0.7)
and sires’ age (r = 0.020, P > 0.8), but it was strictly linked to the size of the litter. Indeed, body mass of animals born in a triplet was significantly lower (df = 14.1, P < 0.001) than that of animal born alone or in pairs, independently of sex (df = 0.09, P > 0.8) and of litter type (df = 1.3, P > 0.2).

Offspring body mass averaged 50.6 ± 0.5 (N = 273 Table 1) 2 months after birth and did not differ between sexes (P > 0.92). It remained however dependent on the size of the litter (df = 11.6, P < 0.001) but not of litter type (P > 0.1) although male offspring born without littermates were significantly heavier (df = 12.3, P < 0.001). Lastly, maternal investment in terms of offspring’s body mass did not depend on dams’ age at conception (respectively P > 0.7 at 30 days, P > 0.8 at 60 days).

Offspring longevity was not linked to their body mass at weaning for both males (r = 0.109, P > 0.2 N = 131) and females (r = 0.111, P = 0.2, N = 135). Likewise the body mass reached by offspring 2 months after birth was unrelated to their lifespan whatever the sex (r = 0.057, P > 0.3, N = 273).

2) Offspring’s longevity and reproductive investment
Among female offspring, no difference in longevity was observed between females that had access to reproduction at least once and those that did not come in contact with males

Table 1. Body mass (g, mean ± E) of female and male offspring at weaning time (30 days) and 60 days after birth depending on litter size.

| Litter size | Females (30 days) | Males (30 days) | Females (60 days) | Males (60 days) |
|-------------|--------------------|----------------|------------------|----------------|
| Single      | 31.9 ± 2.8 (9)     | 34.9 ± 2.2 (13)| 50.8 ± 2.4 (9)   | 58.6 ± 2.2 (13) |
| Pair        | 35.1 ± 0.8 (51)    | 33.5 ± 0.9 (47)| 53.1 ± 1.2 (51)  | 52.3 ± 1.2 (49)  |
| Triplet     | 30.4 ± 0.8 (75)*   | 30.3 ± 0.7 (71)* | 49.3 ± 1.0 (77)* | 47.9 ± 0.9 (74)* |
| Mean        | 32.3 ± 0.6 (135)   | 31.9 ± 0.6 (131)| 50.8 ± 0.8 (137) | 50.5 ± 0.7 (136) |

* Significant differences between triplets and other litters (P < 0.001).
(respectively 5.12 ± 0.2 years, N = 55 versus 5.62 ± 0.2 years, N = 83—df$_{1/136}$ F = 2.71, P = 0.1). By contrast, males having at least one opportunity to mate had significantly longer longevity than the others (respectively 6.04 ± 0.2 years N = 30 versus 4.26 ± 0.3 years, N = 102, df$_{1/138}$ F = 17.6, P < 0.001).

3) Offspring’s longevity and parental age at conception

Dams’ age at conception was negatively correlated to offspring longevity for males (r = —0.309, P < 0.001) but not for females (r = 0.104, P = 0.226—Fig 2). However, Regardless of their sex (P > 0.7), offspring born from 1 year-old dams (primiparous) have a significantly longer longevity than those born from multiparous dams whatever their age (respectively 6.40 ± 0.3 years, N = 67 versus 5.23 ± 0.1 years, N = 211, df$_{1/274}$ F = 14.8, P < 0.001).

Fig 2. Relationship between offspring longevity in males (left panel) and females (right panel) according to the age at conception of dams and sires. Only, a significant correlation was observed between age at conception of dams and longevity in male offspring (r = —0.309, P < 0.001).

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By contrast, the sires’ age at conception did not influence offspring’ longevity for both males ($r = 0.057, P > 0.5$) and females ($r = 0.027, P > 0.8$—Fig 2).

Since sires’ age at conception did not influence the lifespan of offspring, the effect of the parents within a pair on offspring’s longevity would be mainly dependent of the dams’ age. To assess the differential effect of the parents’ age within a pair, we used Cox proportional hazards model with age at conception of both parents as covariate factors. The male offspring longevity was negatively affected by the dams’ age at conception ($P < 0.001$) whatever the sires’ age ($P > 0.9$). The female offspring longevity was independent of sires’ age ($P > 0.5$) and of dams’ age ($P = 0.4$). Whatever the classes of parents’ age (Fig 3), only dams’ age at conception influenced the longevity of offspring (males $df_{1/136}, F = 13.6, P < 0.001$) but not of female offspring ($df_{1/134}, F = 1.4, P = 0.5$). The minimum longevity of male offspring was observed when both parents were old ($P < 0.02$). In addition, when analysing the difference in parental age at

![Fig 3. Lifespan (means ± SEM) of male and female offspring according to the parents’ ages within a breeding pair. The broken line indicates the mean survival (5.5 years).](https://doi.org/10.1371/journal.pone.0265783.g003)
conception, the longevity of male offspring was significantly shorter when dams were older than sires ($r = 0.191$, $N = 140$, $P = 0.024$). No such correlations were observed for female offspring ($r = 0.060$, $P > 0.4$, $N = 138$).

Lastly, when considering the potential relationship between parental longevity and that of their offspring, a significant difference appeared according to sex. The lifespan of male offspring was unrelated to the longevity of their respective mother ($r = 0.006$, $P > 0.9$) and sire ($r = 0.078$, $P > 0.3$). By contrast, the longevity of female offspring correlated significantly with both their mother ($r = 0.168$, $P = 0.048$) and their sire ($r = 0.213$, $P = 0.012$).

Discussion
The longevity of captive mouse lemurs may reach up to 13 years with a 50% survival time around 5.5 years [21, 22] and with no significant difference between sexes. Mouse lemurs are highly seasonal breeders and can reproduce throughout all their life even at an advanced age [19, 28]. Results demonstrated that mothers ‘age at conception affected only the longevity of male offspring while the fathers’ age at conception had no influence on longevity of offspring, whatever their sexes. Like to ruffed lemurs [18], the absence of an effect of fathers’ age suggests that male reproductive senescence is absent in male mouse lemurs. As the mother aged, the survival of male offspring decreased with a minimum when both parents were old. More, as previously described in human [12, 32, 33], only the longevity of female offspring was significantly related to the longevity of both parents.

Among vertebrate species, the effect of mother’s age on pre-adult survival has been well documented [1, 2]. With ageing, a decrease in fertility and in maternal investment is considered to be the key for reduced survival of offspring. Under captive conditions with reduced environmental stress, age does not affect either fertility or maternal investment in female mouse lemurs. As mother age, litter size increases and postnatal growth of offspring remains unaffected. Thus, offspring survival in adulthood is not a result of an inadequate maternal investment or on postnatal conditions in captive mouse lemurs.

In our sample, the mother’s age at conception was negatively correlated with male offspring longevity, but the father’s age at conception had no impact on either sex. This strongly suggests a predominant role of genetic load from the mother.

The effect of parental age on offspring longevity is generally attributed to a direct age-related deterioration of the germ cells: DNA mutation, DNA methylation, shortening of telomeres [34]. Within age-related deteriorations, the telomere length (TL) is recognized as the most suitable biomarker of aging [3] and telomere inheritance appears to be paternal in mammals [4]. A large comparative study on mammalian species, including humans, showed clear relationships between age-related shortening of TL and lifespan [4, 35]. However, the age-related TL shortening appears to be sex- and species-dependent [36–39]. If strong evidence exists for genetic inheritance of TL, conclusions on relationship between parental age at conception and TL of offspring depend on the species studied. In several studies (mostly birds), TL shortens as parents age and predicts offspring TL with sex-specific differences in TL inheritance [6, 8, 40–47]. By contrast, a weak or no relationship between TL and parental TL has been observed in other species [45–48].

Telomere biology in mouse lemurs seems an exception among primates. The average telomere length is among the longest reported for primate species and, no detectable TL shortening with ageing was detectable [49]. Like to hamsters during short day period [50], mouse lemurs use daily torpor, which may contribute to an increase in TL. Moreover, in small-bodied species, the seasonal variation in sperm production might explain the lack of an effect of parental age on TL [46]. In male mouse lemurs, a greater sperm production, the presence of
telomerase activity in testes and social dominance required for successful mating may all contribute to maintenance of TL [51, 52]. Dominant males (i.e. fathers) would invest more heavily in soma reparation and TL maintenance as suggested by the longer lifespan of males that were offered the opportunity to reproduce successfully at least once. All these characteristics could explain the lack of effect of fathers’ age at conception on offspring longevity. Similarly, for female mouse lemurs, the use of torpor, the high reproductive seasonality and the protective role of oestrogens could contribute to TL maintenance over life.

Why mothers’ age at conception affects only male offspring remains however a question. As supported by Entringer et al. 2015 [53], oestrogens levels of the mother would predict TL of offspring. With ageing, levels of oestrogens in female mouse lemurs significantly decrease and male-biased litters are more frequent [54]. But, this decrease does not impact females’ fecundity or female offspring longevity. In humans mitochondrial DNA content is higher in females and no deterioration was observed at advanced maternal age [55]. Thus, offspring from aged mothers would not suffer from lesser portion of maternal genetic load. However, in our study, the lifespan of male offspring from aged mothers have a reduced lifespan compared to those born from younger mothers, whatever the age of the fathers. This sex-specific effect of aged mothers on male offspring longevity could rely to others parameters such as the composition of the litters [56], age-related maternal behaviours or social interactions later in the weaning period. As a consequence, these results could allow better management of the captive colony by removing old females from the breeding pairs and by selecting young females from long-lived lineages.

According to several studies [12, 57, 58], life-history trajectory of offspring could vary according to mothers’ age suggesting potential trans-generational effects of maternal age. For female mouse lemurs, it has been already described that, in the highly favourable conditions of captivity, there was no cost of reproduction for longevity [59]. In several species, offspring from older mothers show changes in their lifetime reproductive success, associated or not with a shorter lifespan [57, 60, 61]. Further work is needed to know whether reproductive success in female mouse lemurs is affected by maternal age at conception. It would be of interest to follow the longevity of all female offspring from a maternal line to decipher the inheritance of female longevity.

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References

1. Monaghan P, Maklakov AA, Metcalfe NB. Intergenerational transfer of ageing: parental age and offspring lifespan. Trends Ecol Evol. 2020; 35, 10.
2. Ivimey-Cook E, Moorad J. The diversity of maternal-age effects upon pre-adult survival across animal species. Proc R Soc B. 2020; 287:20200972. https://doi.org/10.1098/rspb.2020.0972 PMID: 32781953

3. Vaiserman A, Krasnienkov D. Telomere length as a marker of biological age: state-of-the-art, open issues, and future perspectives. Front Genet. 2021; 11:630186. https://doi.org/10.3389/fgene.2020.630186 PMID: 33552142

4. Kappei D, Londoño-Vallejo A. Telomere length inheritance and aging. Mech Ageing Develop. 2008; 129:17–26. https://doi.org/10.1016/j.mad.2007.10.009 PMID: 18054991

5. Bouwhuis S, Vedder O, Becker PH. Sex-specific pathways of parental age effects on offspring lifetime reproductive success in a long-lived seabird. Evolution 2015; 69:1760–1771. https://doi.org/10.1111/evo.12692 PMID: 26095174

6. Criscuolo F, Zahn S, Bize P. Offspring telomere length in the long-lived Alpine swift is negatively correlated to the age of their biological father and foster mother. Biol. Letters 2017; 13:20170188. https://doi.org/10.1098/rsbl.2017.0188 PMID: 28904178

7. Descamps S, Boutin S, Berteaux D, Gaillard J.-M. Age-specific variation in survival, reproductive success and offspring quality in red squirrels: evidence of senescence. Oikos 2008; 117, 1406–1416.

8. Dupont SM, Barbraud C, Chastel O, Delord K, Ruault S, Wermerskirch H, et al. Young parents produce offspring with short telomeres: a study in a long-lived bird, the black-browed albatross (Thalassarche melanophris). PLoS ONE 2018; 13(3):e0193526. https://doi.org/10.1371/journal.pone.0193526 PMID: 29561856

9. Reid JM, Bignal EM, Bignal S, McCracken DJ, Bogdanova MI, Monaghan P. Parental age, lifespan and offspring survival: structured variation in life history in a wild population. J. Anim. Ecol. 2010; 79:851–862.

10. Einsenberg Dan TA, Tackney J, Cawthon RM, Cloutier CT, Hawkes K. Paternal and grandpaternal ages at conception and descendant telomere lengths in chimpanzees and humans. Am J Phys Anthropol. 2017; 162:201–207. https://doi.org/10.1002/ajpa.23109 PMID: 27731903

11. Garcia-Palomares S, Navarro S, Pertusa JF, Hermenegildo C, García-Pérez MA, Rausell F, et al. Delayed fatherhood in mice decreases reproductive fitness and longevity of offspring. Biol Reprod. 2009; 80(2):343–9. https://doi.org/10.1095/biolreprod.108.073395 PMID: 18923156

12. Gillespie DO, Russel AE, Lummaa V. The effect of maternal age and reproductive history on offspring survival and lifetime reproduction in preindustrial humans. Evolution 2013; 67:7:1964–1974. https://doi.org/10.1111/evo.12078 PMID: 23815653

13. Kemkes-Grottenthaler A. Parental effects on offspring longevity: evidence from 17th to 19th century reproductive histories, Annals Hum Biol. 2004; 31:2, 139–158. https://doi.org/10.1080/00324728.2017.1411969 PMID: 29357761

14. Barclay K, Myrskylä M. Parental age and offspring mortality: negative effects of reproductive ageing may be counterbalanced by secular increases in longevity. Population Studies 2018; 72:153–173. https://doi.org/10.1080/00324728.2017.1411969 PMID: 29357761

15. Carslake D, Tynelius P, van den Berg GJ, Smith GD. Associations of parental age with offspring all-cause and cause-specific adult mortality. Sci. Reports 2019; 9:17097. https://doi.org/10.1038/s41598-019-52853-8 PMID: 31745218

16. Hubbard RE, Andrew MK, Rockwood K. Effect of parental age at birth on the accumulation of deficits, frailty and survival in older adults. Age & Ageing, 2009; 38:380–38. https://doi.org/10.1093/ageing/afp035 PMID: 19307228

17. Breton G, Thibault S, Werts M, Baudry E. Captive ring-tailed lemur breeding in semi-free ranging conditions and genetic parental analysis. Zoo Biol. 2019; 38:281–291. https://doi.org/10.1002/zoo.21480 PMID: 30888079

18. Tidière M, Thévenot X, Deligiannopoulou A, Douay G, Whippie M, Siberchicot A, et al. Maternal reproductive senescence shapes the fitness consequences of the parental age difference in ruffled lemur. Proc. R. Soc. B. 2018; 285:20181479. https://doi.org/10.1098/rspb.2018.1479 PMID: 30209228

19. Wright PC, King SJ, Baden A, Jernvall J. Aging in wild female lemurs: sustained fertility with increased infant mortality. In Primate reproductive aging: cross-taxon perspectives (eds. Atsalis S, Margulis SW, Hof PR) 2008; 36:17–28. Basel Switzerland: Karger.

20. Blanco MB, Zehr SM. Striking longevity in a hibernating lemur. J Zool 2015; 296,177–188. https://doi.org/10.1111/jzo.12230

21. Pifferi F, Terrien J, Perret M, Epelbaum J, Blanc S, Picoq J-L, et al. Promoting healthspan and lifespan with caloric restriction in primates. Com Biol. 2019; 2, 107. https://doi.org/10.1038/s42003-019-0348-z PMID: 30911682

22. Languille S, Blanc S, Blin O, Canale CI, Dal-Pan A, Devau G, et al. The grey mouse lemur: a non-human primate model for ageing studies. Aging Res Rev. 2012; 11, 150–162. https://doi.org/10.1016/j.arr.2011.07.001 PMID: 21802530
23. Perret M, Aujard F. Regulation by photoperiod of seasonal changes in body weight and reproductive function in the gray mouse lemur (Microcebus murinus): differential responses by sex, Intern. J. Primatol. 2001; 22:5–24. https://doi.org/10.1023/A:1026457813626

24. Andrè S, Gachot-Neveu H, Perret M. Genetic determination of paternity in captive grey mouse lemurs: local sexual competition rather than sperm competition in a nocturnal prosimian? Behaviour 2001; 138:1047–1063. https://doi.org/10.1163/156853901753286560

25. Andrè S, Solignac M, Perret M. Mating system in mouse lemurs: theories and facts, using analysis of paternity. Folia Primatol. 2003; 74:355–366. https://doi.org/10.1159/000073319 PMID: 14605478

26. Wimmer B, Tautz D, Kappeler PM. The genetic population structure of the gray mouse lemur (Microcebus murinus), a basal primate from Madagascar, Behav Ecol Sociobiol. 2002; 52:166–175. https://doi.org/10.1007/s00265-002-0497-8

27. Zablocki-Thomas PB, Herrel A, Karanewski CJ, Aujard F, Pouydebat E. Heritability and genetic correlations of personality, life-history and morphology in the grey mouse lemur (Microcebus murinus) Royal Soc Open Sci. 2019; 6:190632.

28. Dunlop CE, Telfer EE, Anderson RA. Ovarian germline stem cells. Stem Cell Res Therapy 2014; 5:98. http://stemcellres.com/content/5/4/9828 PMID: 25157949

29. Perret M. Litter sex composition affects first reproduction in female grey mouse lemurs (Microcebus murinus). Physiol Behav. 2019; 208. https://doi.org/10.1016/j.physbeh.2019.112575 PMID: 31176643

30. Huchard E, Canale CI, Le Gros C, Perret M, Henry PY, Kappeler PM. Convenience polyandry or convenience polygyny? Costly sex under female control in a promiscuous primate. Proc. R. Soc. B. 2012; 279, 1371–1379. https://doi.org/10.1098/rspb.2011.1326 PMID: 21976684

31. Behaviour Animal. Guidelines for the treatment of animals in behavioural research and teaching. Anim Behav. 2012; 83:301–309. https://doi.org/10.1016/j.anbehav.2011.10.031

32. Counil A, Legay J-M, Chachter F. Evidence of sex-linked effects on the inheritance of human longevity. A population-based study in the Valserine valley (French Jura), 18–20th centuries. Proc R Soc B. 2000; 267:1021–1025

33. Korpelainen H. Genetic maternal effects on human lifespan through the inheritance of mitochondrial DNA. Hum Heredity 1999; 49, 183–185 https://doi.org/10.1159/000022871 PMID: 10436377

34. Monaghan P, Metcalfe NB. The deteriorating soma and the indispensable germ line: gamete senescence and offspring fitness. Proc. R. Soc. B. 2019; 286:20192187. https://doi.org/10.1098/rspb.2019.2187 PMID: 31847776

35. Gomes NM, Ryder OA, Houck ML, Charter SJ, Walker W, Forsyth NR, et al. Comparative biology of mammalian telomeres: hypotheses on ancestral states and the roles of telomeres in longevity determination. Aging Cell. 2011; 10:761–768. https://doi.org/10.1111/j.1474-9726.2011.00718.x PMID: 21518243

36. Barrett ELM, Richardson DS. Sex differences in telomeres and lifespan, Aging Cell 2011; 10:913–921. https://doi.org/10.1111/j.1474-9726.2011.00741.x PMID: 21902801

37. Eisenberg Dan TA. Paternal age at conception effects on offspring telomere length across species, what explains the variability? PloS Genetics 2019; 15(2):e1007948. https://doi.org/10.1371/journal.pgen.1007946 PMID: 30763310

38. Heidinger BJ, Young RC. Cross-generational effects of parental age on offspring longevity: are telomeres an important underlying mechanism? Bioessays 2020; 42, 19000227. https://doi.org/10.1002/bies.201900227 PMID: 32734707

39. Vedder O, Moiron M, Bichet C, Bauch C, Verhulst S, Becker PH, et al. Telomere length is heritable and genetically correlated with lifespan in a wild bird. Mol Ecol. 2021; 00:1–11. https://doi.org/10.1111/mec.15807 PMID: 33460462

40. Bauch C, Boonkamp JJ, Korsten P, Mulder E. High heritability of telomere length and low heritability of telomere shortening in wild birds. Mol Ecol. 2021; 00:1–16. https://doi.org/10.1111/mec.16183 PMID: 34532917

41. Brown AM, Wood EM, Capilla-Lasheras P, Harrisson XA, Young AJ. Longitudinal evidence that older parents produce offspring with longer telomeres in a wild social population. Biol Letters 2021; 17:2021.10409. https://doi.org/10.1098/rsbl.2021.0409 PMID: 34665991

42. Bouwhuis S, Verhulst S, Bauch C, Vedder O. Reduced telomere length in offspring of old fathers in a long-lived seabird. Biol Letters. 2018; 14(6), 20180213. https://doi.org/10.1098/rsbl.2018.0213 PMID: 29899134

43. Noguera JC, Metcalfe NB, Monaghan M. Experimental demonstration that offspring fathered by old males have shorter telomeres and reduced lifespans. Proc. R. Soc. B. 2018; 285:20180268. https://doi.org/10.1098/rsbl.2018.0268 PMID: 29540524
44. Olsson M, Pauliny A, Wapstra E, Uller T, Schwartz T, Blomqvist. Sex differences in sand lizard telomere inheritance: paternal epigenetic effects increase telomere heritability and offspring survival. PLoS ONE 2011; 6(4):e17473. https://doi.org/10.1371/journal.pone.0017473 PMID: 21526170

45. Froy H, Bird EJ, Wilbourn RV, Fairlie J, Underwood S, Salvo-Chimside E, et al. No evidence of parental effect on offspring leucocyte telomere length in free-living Soay sheep. Sci Reports 2017; 7:999. https://doi.org/10.1038/s41598-017-09861-3 PMID: 28855677

46. Lieshouw van SHJ, Sparks AM, Bretman A, Newman C, Buesching CA, Burke T, et al. Estimation of environmental, genetic and parental age at conception effects on telomere length in a wild mammal. J Evol Biol. 2020; 00:1–13. https://doi.org/10.1111/jeb.13728 PMID: 33113164

47. Sepp T, Meitern R, Heidinger B, Noreikiene K, Rattiste K, Hõrak P, et al. Parental age does not influence offspring telomeres during early life in common gulls (Larus canus). Mol. Ecol. 2021; 00:1–11. https://doi.org/10.1111/mec.15905 PMID: 33772917

48. Sparks AM, Spurgin LG, van der Velde M, Fairfield EA, Komdeur J, Burke T, et al. Telomere heritability and parental age at conception effects in a wild avian population. Mol. Ecol. 2020; 00:1–15. https://doi.org/10.1111/mec.15804 PMID: 33586226

49. Trochet D, Mergei X, Ivkovic I, Porrece RM, Gerbault-Seureau M, Sodibe A, et al. Telomere regulation during ageing and tumorigenesis of the grey mouse lemur. Biochimie 2015; 113:100–110. https://doi.org/10.1016/j.biochi.2015.04.002 PMID: 25882681

50. Turbill C, Smith S, Deimel C, Ruf T. Daily torpor is associated with telomere length change over winter in Djungarian hamsters. Biol Letters 2012; 8:304–307. https://doi.org/10.1098/rsbl.2011.0758 PMID: 21920955

51. Lewin N, Treidel LA, Holekamp KE, Place NJ, Haussmann MF. Socioecological variables predict telomere length in wild spotted hyenas. Biol Letters 2015; 11:20140991. https://doi.org/10.1098/rsbl.2014.0991 PMID: 25716089

52. Wood EM, Capilla-Lasherias P, Cram DL, Walker LA, York JE, Lange A, et al. Social dominance and rainfall predict telomere dynamics in a cooperative arid-zone bird. Mol Ecol. 2021; 00:1–14. https://doi.org/10.1111/mec.15868 PMID: 33657651

53. Entringer S, Epel ES, Lin JL, Blackburn EH, Buss C, Simhan HN, et al. Maternal estriol concentrations in early gestation predict infant telomere length. J Clin Endocri Metab. 2015; 100:267–273. https://doi.org/10.1210/jc.2014-2744 PMID: 25337925

54. Perret M. Relationship between urinary estrogen levels before conception and sex ratio at birth in a primate, the gray mouse lemur, Hum Reprod. 2005; 20:1504–1510. https://doi.org/10.1093/humrep/deh802 PMID: 15790612

55. Mengel-From J, Svane AM, Pertoldi C, Kristensen TN, Loeschke V, Skytte A, et al. Advanced parental age at conception and sex affects mitochondrial DNA copy number in Human and fruit flies. J Gerontol. 2019; A74:1853–1860. https://doi.org/10.1093/gerona/glz070 PMID: 30874797

56. Perret M. Litter sex composition influences competitive performance during first reproduction in male mouse lemurs. Physiol Behav. 2021; 228. https://doi.org/10.1016/j.physbeh.2020.113196 PMID: 33017603

57. Bouwhuis S, Charmentier A, Verhulst S, Sheldon BC. Trans-generational effects on ageing in wild bird population. J Evol Biol. 2009; 23:636–642.

58. Kroeber SB, Blumstein DT, Armitage KA, Reid JM, Martin JGA. Older mother produce more successful daughters. PNAS 2020; 117:4809–4814.

59. Landes J, Henry P-Y, Hardy I, Perret M, Pavad S. Female reproduction bears no survival cost in captivity for gray mouse lemurs. Ecol. Evol. 2019; 9:6189–6198. https://doi.org/10.1002/eece.5124 PMID: 31236213

60. Hayward AD, Mar KU, Lahdenpera M, Lummaa V. Early reproductive investment, senescence and lifetime reproductive success in female Asian elephants. J Evol Biol. 2014; 27:772–789. https://doi.org/10.1111/jeb.12350 PMID: 24580655

61. Schroeder J, Nakagawa S, Rees M, Mannarelli M-E, Burke T. Reduced fitness in progeny from old parents in a natural population. PNAS 2015; 112:4021–4025. https://doi.org/10.1073/pnas.1422715112 PMID: 25775600