Telomere shortening correlates with harsh weather conditions in the bat species Myotis myotis

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Telomere shortening correlates with harsh weather conditions in the bat species *Myotis myotis*

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The relationship of telomere shortening and cellular ageing in cultured cells such as fibroblasts is straightforward: telomeres shorten with an increasing number of cell divisions until they trigger replicative senescence which prevents further mitotic cycles. But studies investigating the relationship between telomere shortening and ageing in whole organisms show contrasting results: while there is a clear decline in telomere length (TL) with chronological age in some species such as humans, no such decline is observed in others. In this issue of Molecular Ecology, Foley et al. (2020) show that experiencing harsh weather conditions correlates with longitudinal telomere shortening in the bat species *Myotis myotis*, whereas chronological age does not (Foley et al., 2020). Further, the authors investigated whether genetics influence TL and find a low heritability (h^2 = 0.01–0.06) again suggesting that environmental effects are the dominant drivers of variation in TL in this species. These are important findings as there is disagreement in the literature about the relative magnitude of genetic and environmental effects contributing to TL variation in different species. This paper investigating the impact of environmental effects makes a novel and important contribution to the literature on TL in free-living mammals.

KEYWORDS

bat, environmental effects, free living mammal, longitudinal telomere change, telomeres, weather

Telomeres consist of noncoding repetitive hexa-nucleotides and associated shelterin proteins and are located at the ends of linear chromosomes. They are widely studied in the biomedical sciences, epidemiology and evolutionary ecology for their potential correlation with cellular ageing, organismal ageing and as markers of past stressors and future survival.

In vitro, it is well understood that telomeres shorten as a result of the so-called end-replication problem where the DNA replication machinery is not able to copy the most ultimate DNA sequence on the lagging strand and as a result it is lost in the daughter strand. When telomeres in a cell become critically short, a DNA damage response is triggered that leads to repair, apoptosis or cellular senescence in a cell-type-dependent manner. Telomere shortening in vitro and in vivo can be accelerated by environmental factors such as oxidative stress. TL in humans is influenced by genetics and the environment, and correlates with future morbidity and mortality (Wang, Zhan, Pedersen, Fang, & Hägg, 2018), and telomere shortening in humans has been recognized as one of the nine hallmarks of organismal ageing (López-Otín, Blasco, Partridge, Serrano, & Kroemer, 2013).

In evolutionary ecology, telomeres have been the focus of many studies which showed that across species and taxa, the relationship between TL and age is far more complicated and does not always show a negative correlation. In some animals, telomere maintenance or even elongation has been found in both cross-sectional

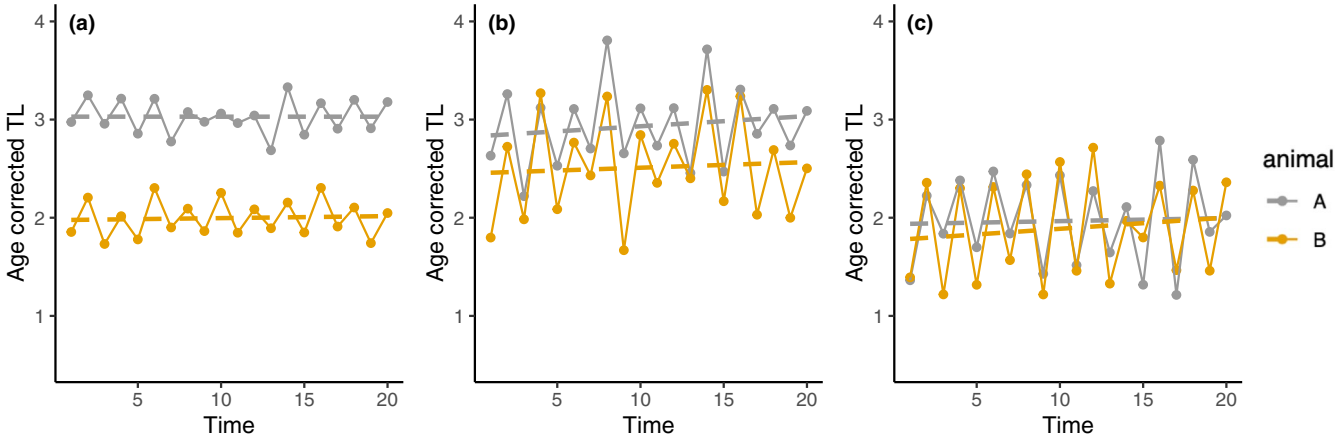

FIGURE 1 Association of environmental and genetic effects on age-corrected telomere length (TL) using simulated data. (a) The variance within animal (true biological change + measurement error) is smaller than the variance between animals (true biological difference in the sum of end telomeric repeats plus interstitial telomeric repeats). Heritability can be measured. (b) The variance between animals is smaller and variance within animals bigger than in the first panel. Heritability estimates are likely to be smaller. (c) No detectable genetic effect on TL, because there is no significant difference in mean TL between animals but a big variance in TL within animals [Colour figure can be viewed at wileyonlinelibrary.com]

and longitudinal studies. Foley et al. have shown previously using a cross-sectional data set that there is no decline in TL with age in the bat species *Myotis myotis* (Foley et al., 2018). In their new study, they have added repeat samples to their data set to investigate individual TL trajectories. Their new results confirm that on average telomeres do not shorten with age in the first six years of life. *Myotis myotis* is a long-lived species (maximum age ~37 years), and the authors concede that a decline later in life may have been missed. Also, it is not practicable to sample very young bats and it may therefore not be possible to measure the initial telomere shortening during the major growth phase that is observed in many other species. The authors find a large variation of TL within age groups which is similar to what has been observed in other species including humans.

Foley et al. also showed that individual trajectories of telomere change are highly dynamic over a period of four years, showing shortening and elongating events independent of age. To better understand factors that influence change in TL over time, the authors hypothesized that weather might be a stressor influencing the trait, because it is known that low temperatures and high precipitation negatively affect nutrition, reproduction and survival in bats. Indeed, they found that more precipitation and lower temperature in spring correlated with more telomere attrition. While weather during other times of the year was investigated, it only had an effect in spring which is known to be a challenging time of the year when bats wake up from hibernation and prepare for parturition. This may indicate that TL maintenance is costly and not prioritized if resources are sparse.

A recent meta-analysis on nonhuman vertebrate species showed an overall effect of environmental stressors on TL (Chatelain, Drobniak, & Szulkin, 2020). However, to date the vast majority of studies investigating environmental effects on TL or change in TL outside the human literature focussed on bird species and comparable studies on wild mammals are rare. Weather effects have been indirectly investigated in two cross-sectional studies: habitat quality correlated with TL in European roe deer with animals living in areas with more precipitation and therefore more food having longer TL at older ages than animals living in a harsher environment (Wilbourn et al., 2017). Similarly, American black bears living at higher latitudes (colder climate) had shorter telomeres (Kirby, Alldredge, & Pauli, 2017). In two longitudinal studies on Soay sheep and European badgers, TL varied with birth cohorts which is likely to reflect yearly variation in environmental conditions such as weather (Fairlie et al., 2015; van Lieshout et al., 2019). Looking at those previous studies, it becomes clear that Foley et al. were the first ones to report an association of precisely measured weather variables and TL in a longitudinal study on adult wild mammals which shows the significance of their work.

While there is evidence that TL is influenced by the environment across different species, there are also studies showing that TL is influenced by genetics. Heritability estimates of TL vary from high in humans to moderate in dairy cattle and are highly variable in free-living birds (Dugdale & Richardson, 2018; Seeker et al., 2018). To calculate heritability in *Myotis myotis*, Foley et al. generated a suite of microsatellite markers and used these to estimate a pedigree. Based on this pedigree, they calculated a very low heritability of $h^2 = 0.01–0.06$ suggesting again that TL is mostly influenced by the environment in this species. Given that the pedigree is less established, it would have been helpful to see a power analysis to confirm that it is suitable to detect higher estimates.

A large heritability can only be found if the variance of TL within individuals is smaller than the variance between individuals (Figure 1). Therefore, if the potentially environmentally driven short-term changes in TL are large, a smaller genetic effect on TL may be masked. Next to true biological change, measurement error may also contribute to TL variation within animals and mask genetic effects. While qPCR (which has been used by Foley et al.) is a very

well-established method for measuring TL and often the only practical method in wild species, there may be some benefit to considering other measurement methods that allow the investigation of absolute TL in kilo bases and are known to have a smaller measurement error. Each time point associated with a large measurement error will affect two adjacent change measurements and therefore measurement error may affect telomere change measurements more than TL measurements. The analysis of absolute TL may have benefits for investigating telomere change within individuals, to compare patterns of change between studies and to allow for more precise heritability estimates.

To better understand the conflicting results of heritability estimates in different species, it may also be helpful to calculate heritability specifically for telomeric repeats that are located at the ends of chromosomes, not for overall TL which usually also includes telomeric sequences located between centromere and telomeres (interstitial telomeres). Interstitial telomeres are likely to contribute to inter-individual variance and to remain more consistent over life than end telomeres and may therefore hugely affect heritability estimates. Perhaps species with large additive genetic effects on TL are simply those that vary more in interstitial telomeric repeats.

Looking at individual species, we see so much variation in TL dynamics with age and with internal and external factors that it is sometimes difficult to believe that we will ever find consistent underlying mechanisms to explain change in TL and their consequences. It may be that different species simply diverged in their evolution and adapted to different TL maintenance strategies to a degree that makes it impossible to find those global similarities. Also, despite all the correlative evidence for telomeres to covary with organismal ageing and other adverse effects including a recent meta-analysis showing that short telomeres are associated with poorer survival in nonhuman species (Wilbourn et al., 2018), a causal link between TL or change in TL and age, morbidity and mortality has not been found to date.

The study by Foley et al. is one of the few investigating the effect of environmental effects on TL in a wild-living mammal and is therefore important. It is also one of few studies reporting heritability estimates for TL in a nonhuman mammal. What remains to be seen is which consequences environmentally driven telomere shortening in *Myotis myotis* has and if it can predict future survival.

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