Comparative insights into telomere biology

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Abstract

Telomeres are conserved DNA sequences that serve as protective caps for linear DNA. Over time, telomeres degrade due to factors including the end-replication problem and oxidative stress. Once telomeres reach a critical length, they initiate a cell signaling pathway resulting in cellular senescence, a hallmark of aging. While telomeres are well-studied in the context of senescence at a cellular level, the relationship between telomeres and organismal longevity is less understood, as most studies focus on within species rather than across species phenomena. Here, we use cross-sectional telomere data from nineteen species to investigate four recent hypotheses in the telomere biology literature: (i) whether the maximum lifespan of a species is associated with either the mean telomere length of that species, or (ii) the telomere loss rates of that species, (iii) whether short telomeres and fast attrition rates play a causal role in aging, as suggested by the telomeric brink hypothesis, and (iv) whether long telomeres are more subject to damage-induced shortening compared to short telomeres. We found that in birds telomere shortening rates (ii), but not mean telomere length (i) relates to species maximum lifespan. In addition, we find no support for the telomeric brink hypothesis (iii) or that longer telomeres are more subject to shortening compared to short telomeres (iv). Our study highlights that comparative data sets can provide powerful insight into the relationship between telomere biology and organismal longevity.

Background

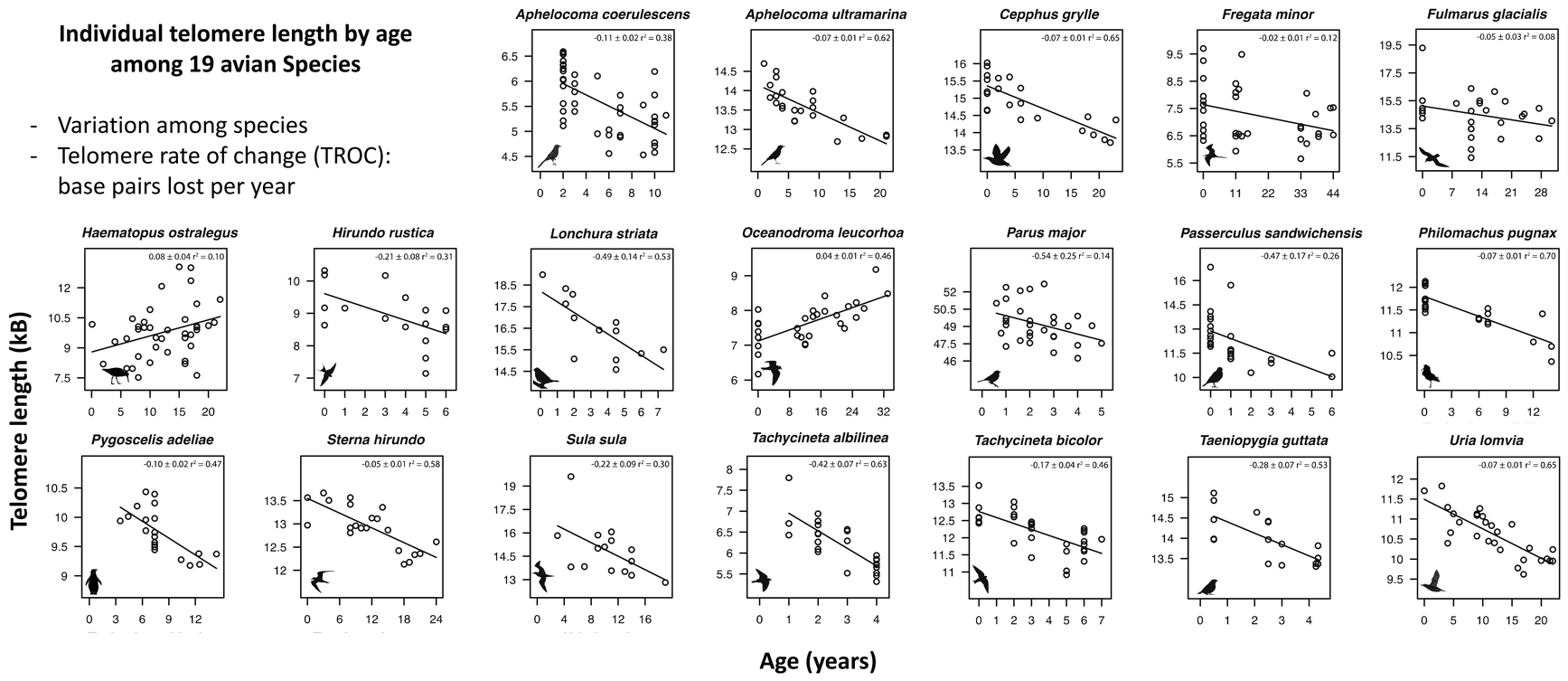
- Telomeres are conserved nucleotide sequences that serve as protective caps on the ends of linear DNA. Telomeres shorten due to the end replication problem and oxidative stress.
- At a cellular level, critically short telomeres result in an altered cell secretory profile and cellular senescence.
- At an organismal level, telomeres are linked to the aging phenotype. Most work is focused within species, and here we explore telomere biology among species to address four recent hypotheses in the literature:
  - I. The rate of telomere loss among species is inversely correlated with their maximum lifespan
  - II. The mean telomere length among species is inversely correlated with their maximum lifespan
  - III. Species with short telomeres and faster shortening rates should have shorter lifespans (the telomeric brink hypothesis)
  - IV. Species with longer telomeres should be more prone to shortening

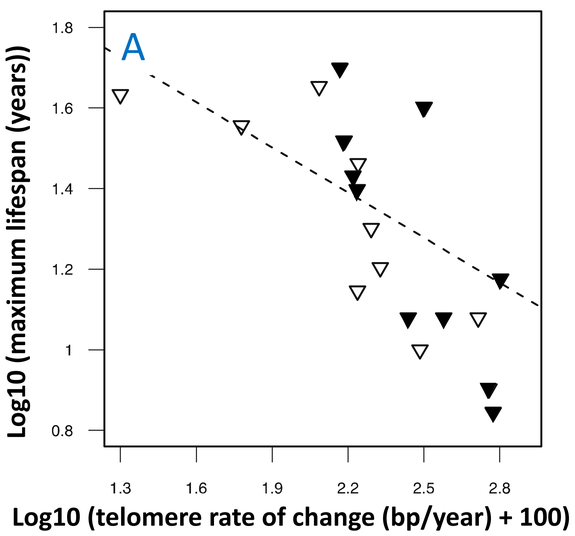
Methods

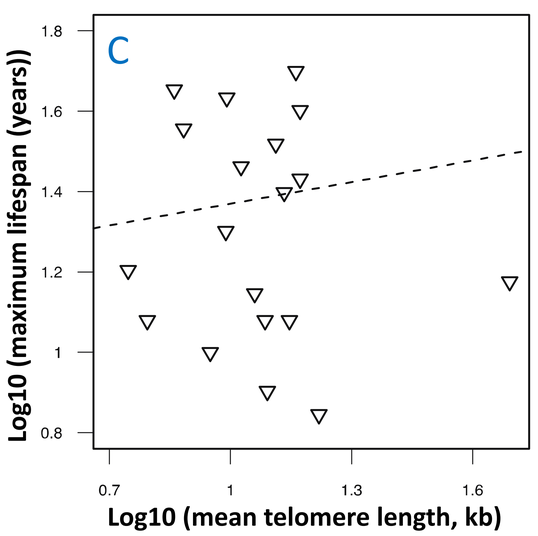
- We measured telomere length in erythrocytes using the Telomere Restriction Fragment (TRF) assay in cross-sectional samples of 19 avian species over their lifespan range.
- Phylogenetically corrected regressions were analyzed using generalized least squares assuming a Brownian correlation structure in package ape in R.

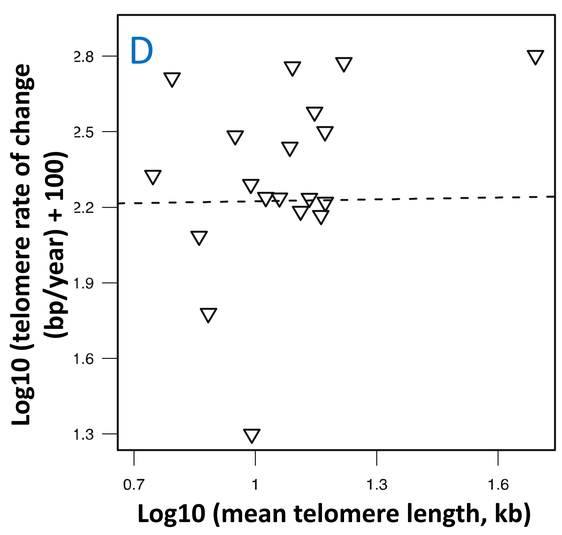
Individual telomere length by age among 19 avian Species

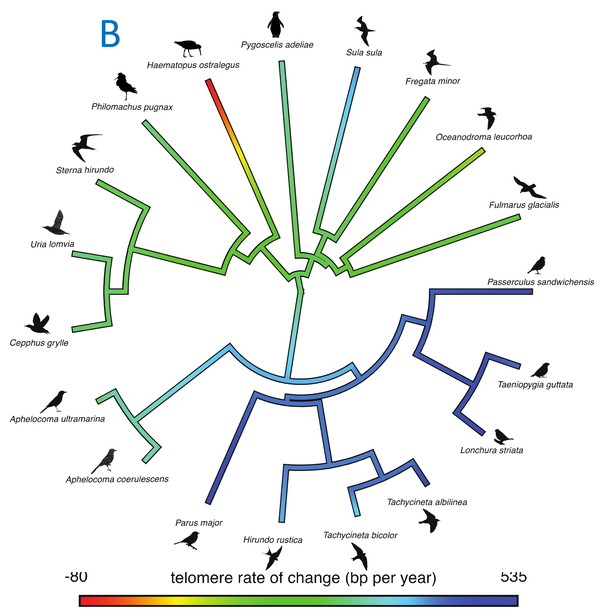
- Variation among species
- Telomere rate of change (TROC): base pairs lost per year











Results and Discussion – Four Hypotheses

Hypothesis 1 (Figure A and B): Telomere loss rates

- Species with longer maximum lifespans have slower rates of telomere shortening.
- Species with longer lifespans may have evolved mechanisms of telomere maintenance to delay senescence.

Hypothesis 2 (Figure C): Mean telomere lengths

- Species with longer maximum lifespans do not have shorter telomeres.
- In mammals, species with longer lifespans have shorter telomeres.

Hypothesis 3 (Figure A – open vs. filled symbols): Telomeric brink hypothesis

- Species with long telomeres (filled symbols) and fast shortening rates do not have shorter lifespans.
- Telomeres may not play a causal role in ageing, but instead serve as a biomarker.

Hypothesis 4 (Figure D): More shortening in long telomeres

- Species with longer telomeres did not have faster attrition.
- Longer telomeres may be more sensitive to damage events, but we do not find support for this across species. Possibly due to variation in telomere maintenance mechanisms.

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