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SYNTHESIS PAPER

Reports of the Death of Extrinsic Mortality Moulding Senescence Have Been Greatly Exaggerated

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Abstract
The classic evolutionary theory of aging posits that senescence evolves because the weakening of selection with age allows mutations with late-acting deleterious effects to accumulate. Because extrinsic mortality is an important cause of weakening selection, the central prediction of the theory has been that higher extrinsic mortality should lead to the evolution of a higher rate of senescence. However, the validity of this prediction has been questioned, even to the extent of suggesting that it is not a prediction of the theory at all, primarily on the basis that changes in population growth rate will compensate for changes in extrinsic mortality. The implication is that empiricists have been using the wrong prediction to test the theory. This claim is misleading, however, because it does not apply on an evolutionary timescale, when population size must be roughly constant. With a constant population size, Hamilton's fitness sensitivities show that extrinsic mortality determines the rate at which the strength of selection declines with age, and thus determines the rate of senescence. The central prediction has been confirmed in the few controlled experiments with model organisms that have been conducted, but clearly this is an area ripe for further investigation.

Keywords Senescence · Ageing · Mutation accumulation · Fitness sensitivity · Population growth · Extrinsic mortality

Introduction

The classic theory of the evolution of senescence or ageing, the decline of physiological condition with age, posits that ageing is inevitable because the strength of selection declines with age. As a result of weakening selection, deleterious mutations expressed at later ages are more likely to accumulate than those expressed at earlier ages, leading to senescence (Medawar 1952; Williams 1957; Hamilton 1966).

Because reduced survivorship with age is an important cause of the decline in the strength of selection, the theory has generally been understood to predict that increasing extrinsic mortality, that is, causes of mortality not connected with senescence, such as predation, disease and accident, will increase the rate of senescence (Williams 1957). This is known as the central prediction because it has been used widely in tests of the theory (Williams et al. 2006). However, the validity of the central prediction has been questioned (Abrams 1993; Caswell 2007; Wensink et al. 2017; Williams et al. 2003; Caswell and Shyu 2017), and it has even been claimed that "…life history theory simply makes no such prediction" (Wensink et al. 2017). This implies a dismal state of affairs in which empiricists have been testing the wrong prediction. Here, I argue that this claim is misleading and show that on an evolutionary timescale increasing the rate of extrinsic mortality should lead to the evolution of a higher rate of senescence.

Wensink et al. (2017) use Hamilton's fitness sensitivities (Hamilton 1966), measures of the relative strength of selection on a mutation expressed at a certain age, to point out that extrinsic mortality is not necessary for senescence to evolve. An easy way to see this is to consider that a lethal mutation expressed before the age of reproduction will not be passed on to the next generation, but one that is expressed only after reproduction has started will be passed on to some extent. Another way to see this is to consider that in a growing population the strength of selection declines with age

Based on the common misquote of Mark Twain's "…the report of my death was an exaggeration." (Fishkin 1996).

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because the continued input of young individuals reduces the proportion of older individuals. Wensink et al. (2017) also point out that, more realistically, with the inclusion of extrinsic mortality, increasing extrinsic mortality does not lead to more rapid senescence because, for a given schedule of fecundity, a decrease in the population growth rate exactly compensates for the greater mortality, leaving the strength of selection at different ages unaffected. These arguments are correct, but misleading. They are misleading because they do not apply to populations of constant size. On an evolutionary timescale, population size must be roughly constant for any population that is not going extinct. Hamilton, in "Returning to a condition of the model which is biologically plausible, indeed the only one which is permanently possible…," considered a constant population size, and, assuming constant fecundity across ages, showed that the intuition of Williams (1957) is correct: an increase in extrinsic mortality is expected to lead to a higher rate of senescence (Hamilton 1966, p. 26).

Hamilton's Fitness Sensitivities

Fecundity

Using the population growth rate r as a measure of fitness, Hamilton (1966) showed that the sensitivity of fitness to a change in fecundity at age a is

$$s'(a) = \frac{e^{(-ra)}l(a)}{T}, \tag{1}$$

where $l(a)$ is the probability of survival from birth to age a, and T is generation time. The term e^{-ra} accounts for the devaluation of reproduction with age when the population size is increasing (or the greater valuation of reproduction with age when the population size is decreasing). With a constant population size ($r=0$), and ignoring generation time because its effect cancels out when considering mutation accumulation (Abrams 1993), this fitness sensitivity becomes

$$s'(a) = l(a). \tag{2}$$

This equation states that the strength of selection on a mutation that changes fecundity at age a is proportional to the probability of survival to that age, which is always a declining function of age. Writing $l(a) = e^{-\mu a}$, where μ is the instantaneous rate of mortality, makes it clear that increasing the mortality rate reduces the strength of selection. Therefore, assuming that most mortality is due to extrinsic causes (Finch 1990), an increase in extrinsic mortality should lead to the evolution of a higher rate of senescence as measured by declining age-specific fecundity.

Mortality

Hamilton (1966) also showed that the sensitivity of fitness to a change in mortality at age a is

$$s(a) = \frac{\sum_{x=a+1}^{\infty} e^{(-rx)}l(x)m(x)}{T}, \tag{3}$$

where $m(x)$ is fecundity at age x. For a population with constant size, and ignoring T, (3) becomes

$$s(a) = \sum_{(x=a+1)}^{\infty} l(x)m(x). \tag{4}$$

Therefore, the strength of selection on a mutation that changes mortality at age a is proportional to expected future reproduction. Future reproduction must always be less than or equal to total reproduction, and with constant fecundity across reproductive ages, expected future reproduction will always decline with age after the onset of reproduction, and therefore the strength of selection will decline with age. With constant fecundity across ages, future reproduction declines at rate μ, and increasingμ should therefore lead to an increase in the rate of senescence. This is true even though fecundity across all ages will increase to compensate for reduced survivorship so that total reproduction equals 1 $\left(\sum_{x=0}^{\infty} l(x)m(x) = 1\right)$, as required for a stable population. Therefore, an increase in extrinsic mortality should lead to the evolution of a higher rate of senescence as measured by increasing age-specific mortality.

Lifetime Reproductive Success

The effect of extrinsic mortality on the rate of senescence is most easily illustrated by assuming fecundity is constant across reproductive ages and by calculating fitness as lifetime reproductive success, which is appropriate for a population of constant size (Charlesworth 1994). In continuous time, mean lifetime reproductive success in a population of constant size is

$$R = \int_{b}^{\infty} e^{-\mu x} m dx = 1, \tag{5}$$

where b is the age of the onset of reproduction. Plotting $e^{-\mu x}m$ against age for different levels of extrinsic mortality, and adjusting m to maintain $R=1$, shows that with high extrinsic mortality expected reproduction is initially higher, but falls off more steeply, than with low extrinsic mortality (Fig. 1). Therefore, the strength of selection declines more

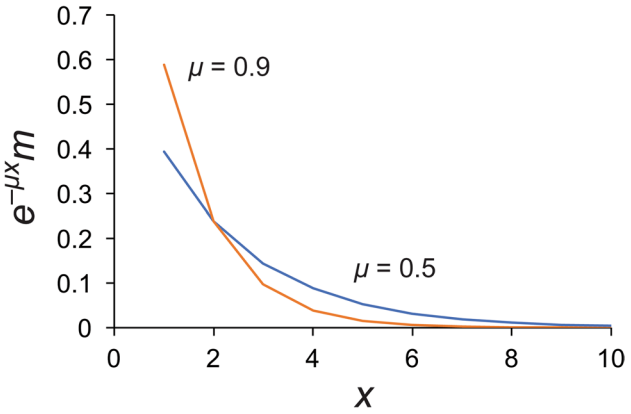

Fig. 1 Expected reproduction at age x for different rates of extrinsic mortality, μ. Fecundity, m, was adjusted to give $R \approx 1$: $\mu = 0.9$ and $m = 1.45$; $\mu = 0.5$ and $m = 0.65$

rapidly with age when the extrinsic mortality rate is higher, causing a higher rate of senescence to evolve. A similar argument is made by Abrams (1993, p. 882).

Abrams (1993) also concludes that an increase in extrinsic mortality leads to more rapid senescence when population size is regulated by density-dependent fecundity. However, he argues that this is not the case if density-dependence acts through intrinsic mortality, since such mortality will decrease to compensate for the increase in extrinsic mortality. This argument relies on the existence of density-dependent intrinsic mortality, that is, that senescent mortality has a density-dependent component.

Empirical Tests

Tests of the central prediction using interspecific comparisons and measurements on wild populations have provided mixed results (e.g., Promislow 1991; Ricklefs 1998), possibly because of the difficulties in measuring extrinsic mortality and senescence in the wild (Williams et al. 2006). Often, presumed correlates of extrinsic mortality, such as flight and arboreality versus terrestrial living (e.g., Shattuck and Williams 2010; Wasser and Sherman 2010), are used rather than direct measures. The ideal test would involve laboratory populations that could be exposed to different levels of extrinsic mortality while controlling for possible confounding variables, such as population density, and for which senescence could be accurately measured. It appears that few such experiments have been conducted. Stearns et al. (2000) conducted an experiment of this type with *Drosophila melanogaster*, and found that higher extrinsic mortality, imposed by random culling, does indeed select for a higher rate of senescence. These results were confirmed with a similar experiment conducted with *Caenorhabditis remanei* (Chen and Maklakov 2012), but gave the opposite result (a lower rate of senescence) when extrinsic mortality was not random, but imposed by heat-shock. Heat-shock is expected to cause "condition-dependent" mortality, such that individuals in better condition have higher survival, which implies selection. If older ages suffer higher extrinsic mortality, because of senescence, this may reduce the rate of senescence. Condition-dependent mortality may be equivalent to density-dependence affecting the survivorship of older individuals more than younger individuals, in which case an increase in extrinsic mortality is expected to reduce the rate senescence (Abrams 1993). Condition-dependent extrinsic mortality has been explored in a formal model and is an area in need of further investigation (Williams et al. 2003). However, extrinsic mortality in natural populations may be mostly condition-independent (Ricklefs 1998).

Conclusion

The claim that the classic theory does not predict an increase in the rate of senescence with an increase in extrinsic mortality is strictly incorrect. With the realistic assumption of a constant population size on an evolutionary time scale, the intuition of G. C. Williams (1957) is correct (Hamilton 1966) and empiricists have not been misguided in using this strong prediction to test the theory.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Research Involving Human and Animal Rights No experiments were conducted in this work.

References

Abrams, P. A. (1993). Does increased mortality favor the evolution of more rapid senescence? *Evolution, 47*(3), 877–887. https://doi.org/10.2307/2410191.

Caswell, H. (2007). Extrinsic mortality and the evolution of senescence. *Trends in Ecology & Evolution, 22*(4), 173–174. https://doi.org/10.1016/j.tree.2007.01.006.

Caswell, H., & Shyu, E. (2017). Senescence, selection gradients, and mortality. In R. P. Shefferson, O. R. Jones & R. Salguero-Gómez (Eds.), *The evolution of senescence in the tree of life* (pp. 56–82). Cambridge: Cambridge University Press.

Charlesworth, B. (1994). *Evolution in age-structured populations. Cambridge studies in mathematical biology* (Vol. 13, 2nd ed.). Cambridge: Cambridge University Press.

Chen, H., & Maklakov, A. A. (2012). Longer life span evolves under high rates of condition-dependent mortality. *Current Biology, 22*(22), 2140–2143. https://doi.org/10.1016/j.cub.2012.09.021.

Finch, C. (1990). *Longevity, senescence, and the genome (The John D and Catherine T MacArthur Foundation series on mental health and development)*. Chicago: University of Chicago Press.

Fishkin, S. F. (1996). *Lighting out for the territory: reflections on Mark Twain and American Culture*. Oxford: Oxford University Press.

Hamilton, W. D. (1966). The moulding of senescence by natural selection. *Journal of Theoretical Biology, 12*(1), 12–45.

Medawar, P. B. (1952). *An unsolved problem of biology*. London: H. K. Lewis.

Promislow, D. E. L. (1991). Senescence in natural populations of mammals: A comparative study. *Evolution, 45*(8), 1869–1887. https://doi.org/10.2307/2409837.

Ricklefs, R. E. (1998). Evolutionary theories of aging: Confirmation of a fundamental prediction, with implications for the genetic basis and evolution of life span. *The American Naturalist, 152*(1), 24–44. https://doi.org/10.1086/286147.

Shattuck, M. R., & Williams, S. A. (2010). Arboreality has allowed for the evolution of increased longevity in mammals. *Proceedings of the National Academy of Sciences, 107*(10), 4635–4639, https://doi.org/10.1073/pnas.0911439107.

Stearns, S. C., Ackermann, M., Doebeli, M., & Kaiser, M. (2000). Experimental evolution of aging, growth, and reproduction in fruitflies. *Proceedings of the National Academy of Sciences, 97*(7), 3309–3313, https://doi.org/10.1073/pnas.97.7.3309.

Wasser, D. E., & Sherman, P. W. (2010). Avian longevities and their interpretation under evolutionary theories of senescence. *Journal of Zoology, 280*(2), 103–155. https://doi.org/10.1111/j.1469-7998.2009.00671.x.

Wensink, M. J., Caswell, H., & Baudisch, A. (2017). The rarity of survival to old age does not drive the evolution of senescence. *Evolutionary Biology, 44*(1), 5–10. https://doi.org/10.1007/s11692-016-9385-4.

Williams, G. C. (1957). Pleiotropy, natural selection, and the evolution of senescence. *Evolution, 11*(4), 398–411.

Williams, P. D., Day, T., Fletcher, Q., & Rowe, L. (2006). The shaping of senescence in the wild. *Trends in Ecology & Evolution, 21*(8), 458–463. https://doi.org/10.1016/j.tree.2006.05.008.

Williams, P. D., Day, T., & Morgan, M. (2003). Antagonistic pleiotropy, mortality source interactions, and the evolutionary theory of senescence. *Evolution, 57*(7), 1478–1488. https://doi.org/10.1554/02-606.