

How can evolutionary theory accommodate recent empirical results on organismal senescence?

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Abstract According to a prominent recent report, guppies collected from sites lacking predators are inferior in every aspect of their life history profile to those evolved in other, nearby sites with predators present. This is an exception to two classical predictions of evolutionary theory: that low extrinsic mortality should be associated with longer life span, and that higher fertility should be associated with shorter life span. Some theorists have tried to accommodate this and other anomalous results within the standard framework, but we argue that the exceptions they carve out do not explain the results at hand. In fact, the findings suggest that population regulation has been selected at the group level, though this is a mechanism that most theorists regard with suspicion. We conclude by relating the present result to other experiments that seem to point in the same direction.

Keywords Group selection · Aging · Guppies · *Poecilia reticulata* · Life history theory · Reproductive potential

Since Weismann gave up his early invocation of group selection, all evolutionary theorists who have published on the causes of aging have agreed that the ultimate cause is the declining force of natural

selection with age. This is the essential evolutionary theory of aging... [A]ging is a straightforward corollary of population genetics theory.... That does not show that the evolutionary theory of aging is correct. That must be decided empirically.

- Rose 1991 (p. 16).

Introduction

Reznick et al. (2004) recently reported striking results from an experiment in which life history traits of guppies collected from the wild were measured in captivity. Guppies collected from stream environments lacking predators were found to be inferior in every aspect of their life history profile to those evolved in other, nearby sites with predators present. This is an exception to two classical predictions of evolutionary theory: that low extrinsic mortality should be associated with longer life span, and that higher fertility should be associated with shorter life span (Williams 1957).

Evolutionary theories of life history derive from the postulate that natural selection tends to optimize individual reproductive success (Charlesworth 1994; Stearns 1992). Different fertility and longevity profiles are conventionally explained in terms of responses to tradeoffs available in contrasting environments. But how can we make sense of a situation where all the advantage is found on one side of the trade, as seems to be the case in Reznick's results?

In this paper, we review some theoretical approaches that might seem to account for the anomaly, and find none that are entirely satisfactory. In fact, Reznick et al.'s recent results add to a body of experiments that have falsified basic predictions of the standard theory. All these anoma-

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lies can be resolved in a theory that regards senescence as a group-level adaptation for population regulation. While recognizing that this view poses theoretical dilemmas, we outline the case for such an interpretation.

Background

When Williams (1957) first formulated the Antagonistic Pleiotropy (AP) hypothesis for the evolution of senescence, he explicitly predicted that higher levels of adult mortality (e.g., through predation) should lead to lower selection pressure at late ages, and consequently to shorter life spans. His reasoning was straightforward and cogent. The prediction has been applied as a test of the AP hypothesis, and results in accordance with the prediction have been cited in its support (Austad and Fischer 1991; Austad 1993, Keller and Genoud 1997; Ricklefs 1998). Although these early studies supported the AP hypothesis, more recent studies have failed to find the predicted pattern (Gray and Cade 2000), or have even found the opposite of the predicted pattern (Miller et al. 2000, 2002; Reznick et al. 2001).

In another contradiction to theoretical predictions, Abrams (1993) noted that empirical data from mammalian life tables included cases where intensity of predation was positively correlated with life span. To address this problem, he undertook a detailed mathematical analysis of the effects of mortality on the evolution of senescence. In formulating predictions of the AP hypothesis, Williams (1957) had discussed the effects of “adult mortality”. However, to resolve an apparent tautology in the way that Williams had originally phrased his hypothesis, Abrams reframed Williams’ hypothesis as “the idea that (senescent) mortality increases with increasing *extrinsic* mortality”. (Emphasis added). Moreover, Abrams studied the “simplest case” in which extrinsic mortality was defined as being absolutely independent of age or condition. Under this simplifying assumption, Abrams found that extrinsic mortality should be considered a broadly neutral force with respect to evolving life history characteristics. He studied two cases: that in which population growth is density-independent, and that in which population growth is density-dependent. He concluded that in the first case, increased extrinsic mortality should have no effect on the rate of senescence, and in the second case, it could either increase or decrease the rate of senescence, depending on the nature of population regulation. Although he suggested that these results were relevant to understanding the evolution of senescence, and to testing the AP hypothesis, Abrams also noted that the assumption of age-independent extrinsic mortality seldom obtains in natural populations: “There has never been any demonstration that a major mortality factor of a natural population is completely independent of

age... Mortality that is totally extrinsic may be rare”. When Abrams relaxed the assumption of strictly age-independent mortality, he concluded that mortality rate can have a wide variety of effects on rate of senescence, depending on various other assumptions. He summarized thus: “It is possible that higher extrinsic mortality will increase the rate of senescence at all ages, decrease the rate at all ages, or increase it at some ages while decreasing it at others”. He also noted that in contrast to Williams’ considerations of adult mortality, predation concentrated on juveniles may actually retard senescence.

Although Abrams’ complex and varied mathematical models did not always conform to the pattern predicted by Williams, it is not clear what practical import this has for testing the AP hypothesis. Abrams himself did not make any explicit claim that Williams’ predictions were not valid for natural populations. We argue that the same predictions of Williams that were taken to support the AP hypothesis when they agreed with empirical results should also be taken to falsify the hypothesis when they fail to match empirical results.

Williams and Day (2003) also have delineated an exception to the expectation that lower mortality from predation should tend to evolve longer life span. Their model is based on interactions between intrinsic and extrinsic mortality, such that individuals that have been weakened by senescence are most vulnerable to predation and disease. Because this model is concerned with susceptibility to predation as an influence on fitness, its predictions are not directly applicable to the study by Reznick et al. (2004). Reznick’s experimental method was to capture fish from different environments, then measure their life spans in a laboratory tank, free of predators and disease. The Williams and Day model would predict that those guppies that were long-lived in the predator-infested native environment would do poorly in a laboratory tank, because selection would have caused them to trade away their (truly) intrinsic longevity for the speed and agility they need to evade predators in the wild. Thus the proposed interaction between intrinsic and extrinsic mortality sources does not help to explain Reznick’s paradoxical results.

Both the analyses of Abrams (1993) and of Williams and Day (2003) were presented as mathematical abstractions. The mathematics tends to obscure the corresponding ecological conditions, leaving the impression that evolutionary theory makes no clear predictions in this area. We maintain that the original predictions of Williams were sound and quite general. They depend only on the postulate that natural selection optimizes individual reproductive success. Under most circumstances in nature, including the likely conditions of Reznick’s collection sites, increased predation should be expected to weaken selection pressure for longer life, so that under any of the currently accepted

evolutionary theories, intrinsic life span should decrease in response. The observed association of higher fertility with longer life span compounds the difficulty of explaining Reznick results within the compass of AP theory.

Verbal reasoning in support of the Williams prediction

Intuitively, Williams's (1957) prediction regarding the effect of predation on intrinsic senescence is easy to understand: His theory of aging was based on pleiotropy that links benefits early in life to costs that manifest as mortality later in life. Higher predation rates increase extrinsic mortality, which decreases the probability that prey individuals will live long enough to pay the cost of these tradeoffs. Since the benefits of early survival and fertility are relatively unaffected by predation, these pleiotropic adaptations offer a net fitness gain under high predation conditions, and we expect that they will more often be selected. This same basic insight applies to all currently popular theories for the evolution of aging, and is traceable to Medawar's (1952) observation that selection pressure for any fitness component declines over an individual's life span, precisely because extrinsic mortality makes the latter part of the life span irrelevant to some subset of individuals.

A numerical example of the AP trade-off

The fitness of a life history is conventionally calculated as the Malthusian parameter r , which is defined implicitly by the Euler-Lotka equation in terms of survival and fertility:

$$\int e^{-rx}l(x)b(x) = 1$$

(Fisher 1930; Rose 1991), where $l(x)$ is the probability of surviving to age x , and $b(x)$ is the effective fertility of an x -year-old. This equation cannot be solved algebraically, but numerical computation of r is straightforward. In the special case where mortality m and fertility b are both constant, the function $l(x)$ takes the form e^{-mx} , and r may be calculated exactly as $r = b - m$, a simple and satisfying result.

For a quantitative example of the tradeoff envisioned by Williams (1957), consider Fig. 1, which depicts expected reproductive output across the life span in two identical populations that inhabit different environments. Both fertility and mortality are constant functions of age in this simplest case. Age profiles are declining exponentials. In the high-predation environment (grey curve), the profile declines more steeply with age. (In this illustration, the coefficient of exponential decline is twice as great for the grey curve as for the black one.)

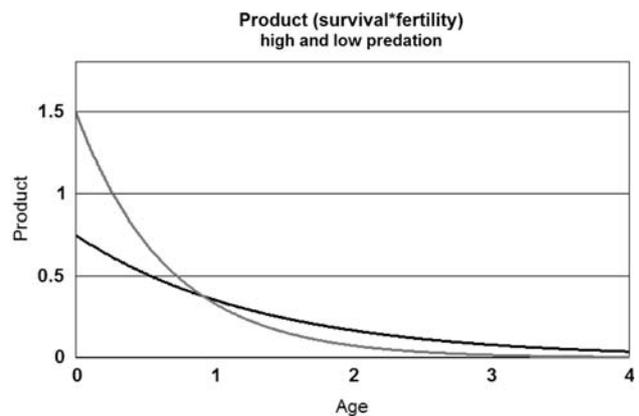


Fig. 1 The product of survival \times fertility across the age distribution is charted for two hypothetical populations, one (grey line) with higher mortality and higher fertility, the other (black line) with lower mortality and lower fertility. The area under each curve is unity, corresponding to $R_0 = 1$ in steady state

We have assumed a fertility rate for the high-predation population that is twice that of the low-predation population. High mortality leads to low population density, and thus greater per capita food availability which supports a higher fertility. This negative feedback on population growth rate causes populations to stabilize in size, and thereby to persist indefinitely.

Now imagine that there exists a pleiotropic allele that trades off longevity for fertility. To be specific, imagine that the allele enhances fertility by 10%, but causes sudden death at age 2. (This example is based on fixed life span rather than gradual onset of senescence merely for computational convenience; this feature is not essential to the reasoning. With a truncated exponential for $l(x)$, it is a simple matter to compute r exactly.)

Values of r are calculated easily for the simple example of a declining exponential, where $l(x) = e^{-mx}$. The first column of Table 1 compares the grey lines in Figs. 1 and 2; the second column compares the black lines in the same two figures. The calculation demonstrates that trading away intrinsic longevity in exchange for higher fertility is a winning proposition in the High Predation column, but is a losing proposition in the Low Predation column.

The loss of the late-life contribution to fitness is more significant to the low-predation life history (grey lines). For this population, the tradeoff will not be worthwhile, and the pleiotropic allele will not be selected. In contrast, the late-life contribution to fitness is much smaller for the high-predation life history (black lines). In this population, the tradeoff carries a net benefit, and we expect that the pleiotropic allele will be positively selected.

(Note: If you think intuitively in terms of the areas under these curves (R_0) as a measure of fitness, you get the same qualitative result. R_0 is the total number of offspring pro-

Table 1 Values of life history variables corresponding to Figs. 1 and 2

	High predation	Low predation
Full life span, low fertility	$b = 1.5; m = 1.5; r = 0; R_0 = 1$	$b = 0.75; m = 0.75; r = 0; R_0 = 1$
Truncated life span, high fertility	$b = 1.65; m = 1.5; r = +0.080; R_0 = 1.045$	$b = 0.825; m = 0.75; r = -0.20; R_0 = 0.855$

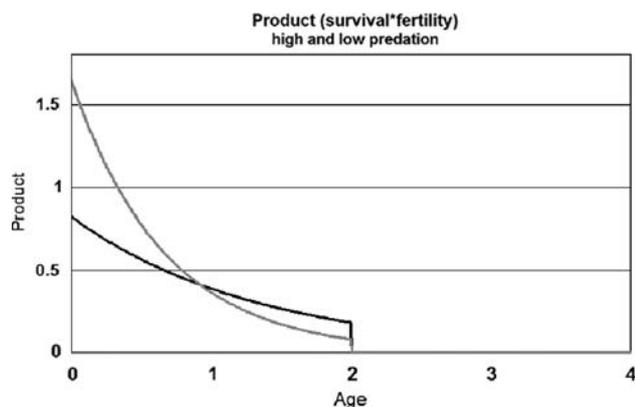


Fig. 2 The populations in Fig. 1 are subject to a life history tradeoff that offers 10% higher fertility in return for ‘senescence’ that induces sudden death at age = 2. As in Fig. 1, the *grey line* represents a population in which extrinsic mortality occurs at twice the rate as the population represented by the *black line*

duced. The measure of fitness that we are using here is the more standard quantity r , which weights earlier reproduction more heavily.)

Is predation mortality neutral with respect to evolution of longevity?

The foregoing numerical example is precisely in accord with the situation as Williams (1957) envisioned it when he proposed the pleiotropic theory of aging. Nevertheless, Abrams (1993) calculates that mortality that affects all ages equally (as we have assumed above) will be neutral with respect to selection for life span characteristics, if population growth is density-independent. What is the origin of this difference in predictions?

The result of Abrams may be technically sound, yet biologically unimportant. If population growth is density-independent, it follows that when a previously stable population is subjected to increased external mortality this will not be offset by increased fecundity, and the population will consequently decline toward extinction. For understanding the evolution of senescence, it is of little interest what selective pressures come to bear on a population as it approaches extinction. Alternatively one could assume that prior to increased external mortality, the density-independent population was not at equilibrium, but

was growing unconstrained, exponentially, at its maximal intrinsic rate. Again, this situation is mathematically tractable, but biologically unrealistic for any population persistent enough to be evolving.

The argument from genotype by environment interaction

One more mechanism that might seem to reconcile the findings of Reznick et al. (2004) with life history theory is the idea that the presence of predators increases the payoff for speed and agility (Williams and Day 2003). Since loss of speed and agility is part of the aging process, and since the presence of predators increases the penalty for this loss, it was argued that predation might induce a transition to longer life spans by motivating the maintenance of youthful speed for a longer period.

But this suggestion is not consistent with the AP hypothesis. The AP hypothesis posits that the deficits characteristic of the latter part of the life span are caused by the trading away of late survival and fecundity for early survival and fecundity. The presence of predators certainly selects for increased speed and agility for their evasion; but according to the AP hypothesis, traits that bring a fitness benefit at one age also bring a fitness cost at another age. If predators select for speed and agility late in life, this must entail either no antagonistic trade-off at all, or else involve the trading away of early fitness in exchange for later fitness. Thus the suggestion of Williams and Day does not help us to reconcile the findings of Reznick et al. (2004) with the AP hypothesis. As noted above, it also does not apply to life spans measured in captivity (as in Reznick’s experiment).

Hint of a group selective mechanism from translocation experiments

Bryant and Reznick (2004) introduced guppies drawn from a high-predation stock into a neighboring low-predation site. Everything we know about life history theory suggests they would out-compete the guppies that were native to that site: Their speed and agility for escaping predators were of little use in the new environment, but their higher fertility and longer reproductive life span assured that their

variety would dominate competition. One of the outcomes that they mention is an outbreak of a disease that had not previously been observed in the high-predation site, less than a hundred meters distant. Another unexpected infectious outbreak was reported by Endler (1980) under similar experimental conditions. We suggest that these observations are consistent with a group-selective mechanism, in which infectious epidemics favor modest population densities. In an environment where infectious disease provides a powerful incentive for population densities to remain modest, it is possible for limits on life span to evolve as an adaptation (Mitteldorf and Pepper 2007).

Conclusion

It is difficult to make sense of Reznick et al.'s (2004) result within the context of a theory based exclusively on individual selection, invoking either a tradeoff or mutational load. Guppies from the low-predation site are producing about half as many offspring as those from the high-predation site; they are producing them later; they are dying earlier; their maximum swimming speed is reduced. It is not plausible that they are maximizing their reproductive success, or any common measure of individual fitness. If some pleiotropic effect has induced these low-predation guppies to trade away these cardinal life history characteristics, then what can it be that contributes so powerfully to their fitness as to justify such a trade?

We have theorized elsewhere (Pepper and Smuts 2000; Mitteldorf 2006) that the volatility of local population dynamics can be an important force in evolutionary ecology. The advantage of restraining violent fluctuations in population size can be a major component of fitness, able to oppose and balance the imperative to maximize individual reproductive potential. In the present situation, it appears likely that small subpopulations are in danger of growing dense enough to trigger starvation or epidemics that threaten local extinction. This is a group selection process to be sure, but of a type that can be swift and efficient, especially in a structured population, such as that of guppies in multiple semi-isolated pools.

Senescence may evolve because it keeps population growth rates in check. This is a conclusion that makes no sense in the context of purely individual-level selection. But excessive growth can lead to demographic catastrophe for a subpopulation, if population growth rate substantially exceeds the corresponding growth rate for populations of food species (Mitteldorf 2006). Local extinctions may effect selection for a higher rate of senescence that complements lower extrinsic mortality.

Epidemic outbreaks are another highly non-linear effect creating selection pressure for limited population size.

Elsewhere, (Mitteldorf and Pepper 2007) we have noted that the advantage of keeping infectious outbreaks in check is a well-recognized evolutionary force in the context of the evolution of sex (Bell 1982). This is an application of the *Red Queen Hypothesis* (van Valen 1973). Application of the Red Queen to explain the evolution of senescence seems a justifiable extension to its accepted scope, and in Reznick's observations of guppies, we may be directly observing the selective pressure that can be imposed by infectious disease in a structured population.

It is generally believed that natural selection among individuals within a population is much more effective than selection among populations. Any radical departure from the way that we have supposed natural selection to work should not be entertained in response to any one experiment. If Reznick's result were an isolated aberration, it would be wildly speculative to discard basic tenets of population genetic theory. But in fact there is a large body of experimental contradictions to both the pleiotropic theories and mutation accumulation, emerging in recent years at an accelerating pace (Bredesen 2004; Mitteldorf 2004). In genetic experiments, single genes have been identified in which mutations can substantially extend life span in every species where they have been sought. Breeding of flies for longevity has led to the paradoxical result that fertility is simultaneously enhanced (Leroi et al. 1994). And contrary to all expectation, evolutionarily conserved families of aging regulators have been identified in widely-separated eukaryotes from yeast to man (Kenyon 2001).

Perhaps Reznick's long-lived guppies are most readily understood in the context of a body of experimental data that points toward the need for a basic shift in thinking about life history evolution, and the relative importance of individual fitness versus ecologically-driven selection among populations.

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