Life-prolonging measures for a dead theory?

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Abstract In a recent review article, Selman and colleagues (Trends Ecol Evol 27:570–577, 2012) discuss the status quo of the oxidative stress theory of aging (OSTA) and how it links to life history evolution. They suggest that the OSTA should be tested in wild populations which might show effects masked in laboratory settings. We disagree with their propositions for several reasons. We argue that there is increasing evidence that reactive oxygen species (ROS) are not causally linked with aging and that ROS do not play a straightforward role in shaping life history evolution. We propose that laboratory animals and semi-wild populations rather than wild animals are suited best to test any hypothesized effect of reactive oxygen species. This is because data from controlled manipulative experiments rather than observational correlations are preferred to solve this issue. In addition, nonconventional model organisms will be useful in answering the question how relevant the OSTA could be for life history evolution.

Keywords Oxidative stress theory of aging (OSTA) · Aging theories · Model species · Life history · Mitohormesis · Invertebrates

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Selman and colleagues (2012) recently discussed the status quo of the oxidative stress theory of aging (OSTA) and how it links to life history evolution. In short, OSTA posits that reactive chemical agents damage cellular structures, including DNA, and that these damages cause aging and ultimately death (Selman et al. 2012). According to the disposable soma theory, there is a trade-off between soma maintenance and reproduction (Kirkwood 1977). Short-lived organisms are predicted to neglect oxidative damage, whereas longer-lived organisms should trade off fertility and protection against oxidative damage. However, there is increasing evidence that reactive oxygen species (ROS) are not causally linked with aging (Pérez et al. 2009). Selman et al. (2012) agree, yet argue that there might still be a role of oxidative damage in shaping life history and suggest that this would only be measureable in the wild. We disagree with this proposition, based on the aforementioned published data (e.g., Buffenstein 2008; Buffenstein et al. 2008; Voituron et al. 2011), and argue that controlled laboratory experiments are better suited to test the hypothesized link between oxidative damage and life history evolution.

Oxidative damage per se seems to have a little influence on longevity (Buffenstein 2008), and only severe damage, such as that caused by high concentrations of paraquat, will reduce life-span (Fujii et al. 2005).

What, then, are the functions of antioxidative mechanisms, if they do not contribute to longevity in the way it has been assumed in the past? To what extent could they shape life history traits, and how? Unfortunately, Selman and coauthors (2012) do not suggest alternative modes of action, which life history decisions, specifically, could be

affected, and which mechanisms might be involved. A relatively new hypothesis is (mito)hormesis, which suggests that naturally occurring low concentrations of ROS function as signaling molecules in longevity pathways but are not the cause of aging (Ristow and Zarse 2010).

Should we, maybe, discuss “health span” rather than life-span? After all, senescent individuals in the wild seldom die peacefully of old age but rather suffer from an associated increased mortality risk (but see Baudisch and Vaupel 2012). It is this survival rate or, more precisely, its associated inclusive fitness that is selected to be maximized. If ROS have a negative effect on longevity and reproductive success, one would predict that individuals with a high fitness should have low levels of ROS. To our knowledge, this has not yet been tested.

Skeptics have raised doubts about the validity of experiments based on small, short-lived organisms in the laboratory. They argue that even if oxidative damage per se does not influence longevity under ideal conditions, it might significantly reduce survival when faced, e.g., with competitors, predators, limited food resources, or diseases. This might be mediated, for instance, by a reduced immune function and decreased sensing or fighting abilities. However, several examples of long-lived animals in the wild that falsify the OSTA are known (e.g., Buffenstein 2008; Buffenstein et al. 2008; Voituron et al. 2011). While we agree that more data are needed, we propose that these should not be gathered in the wild. Rather, we suggest that experimentation in laboratories or under closely monitored seminatural conditions would yield the most conclusive results. Controlled settings allow for systematic manipulation and evaluation of the factors involved, including genetic diversity. In addition, relevant parameters can be repeatedly assessed in the same individuals. To evaluate the impact of suboptimal conditions on oxidative stress and aging, harsh experimental treatment might be needed, such as malnutrition, exposure to parasites and diseases, extreme temperatures, or social stress. Evidently, such experiments implicate considerable ethical issues that require a sensible ethical debate.

To address the abovementioned concerns, it might be advisable to use larger animals, such as guinea pigs and rabbits. Instead of studying lab-raised zebra finches where artificial selection for fecundity might have altered traits involved in aging, recently, wild-caught birds should be investigated (compare Harper 2008). Additional insights from nonstandard model organisms,

such as budgerigars, other birds (Holmes 2004), or fish (Gerhard 2007), will also prove valuable. Potentially, research on semi-wild populations of goats, sheep, deer, or fish could add to the understanding of patterns of oxidative damage and life history decisions.

Currently, it seems that nothing is sure anymore in aging research, and therefore, it is maybe the right time to take leave of dear held theories and develop new approaches to answer the questions raised by Selman et al. (2012).

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