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Non-evolutionary and Evolutionary Aging Theories

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Synonyms

Evolutionary aging theories; Non-evolutionary aging theories; Programmed aging theories

Definition

The distinction in two groups of aging theories, non-evolutionary and evolutionary, derives from the non-consideration or consideration, respectively, of the evolutionism in the requirements of a theory. Here, this distinction is studied in depth. Moreover, it is observed that, within the group of evolutionary theories, some attribute, in evolutionary terms, always a negative value to aging and reach conclusions similar to those of non-evolutionary aging theories. On the contrary, other theories attribute to aging a positive value in particular conditions and come to widely different conclusions.

Overview

Before the Darwinian hypothesis of evolution by natural selection (Darwin 1859), and also for a long time thereafter, aging has been considered by many theories as the inevitable effect of wear and tear phenomena and of the accumulation of harmful metabolic substances (Comfort 1979; Medvedev 1990). In the older theories of these group, which on the whole may be defined as "damage accumulation hypotheses" (Libertini 2015, p. 56), aging is explained as the effect of mechanical wear or of various types of biochemical damage (e.g., toxic metabolites, harmful substances produced by intestinal bacteria, cosmic rays, mechanochemical deteriorations in cell colloids) or of progressive tissue degeneration (e.g., changes in specific nervous/endocrine/vascular/connective/other tissues and organs) (Comfort 1979; Medvedev 1990; Höhn et al. 2017; Ogrodnik et al. 2018). The newer hypotheses of this group propose that aging is caused by cumulative damage due to oxidative effects of free radicals on DNA/mitochondria/whole body or to DNA transcription errors (Libertini 2015).

A different theory interpreted aging as a consequence of the cessation of somatic growth. In fact, while senescence is evident in animals that show somatic growth only up to a certain age, aging is not evident for species, as many fish, where there is constant capacity for growth (Bidder 1932): "[Bidder] pointed to a number of

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instances in fish where constant expectation of life, capacity for growth, and general vigor appeared to persist indefinitely" (Comfort 1979, p. 14). The interesting point of this theory is that it somehow tried to explain the absence of detectable aging in fish, while the other theories did not give a justification for this evidence.

Before 1950, the only exceptions to this concept of aging were two insights that were not deepened. Alfred Russel Wallace, the co-author with Charles Darwin of the first paper on evolution through natural selection, observed that individuals who die as a consequence of aging do not compete with their offspring and proposed this as an explanation for aging (Wallace 1865–1870). Some years later, August Weismann hinted that aging was somehow favored by natural selection because the death of old individuals frees space for the younger generations and so for the spread of new genes (Weismann 1889).

However, these ideas were disregarded and the same Weismann repudiated his proposal (Weismann 1892).

After this time, some theories were proposed that somehow tried to frame the aging phenomenon in the context of the mechanisms of natural selection. The main theories of this group are (Libertini 2015):

- *Mutation accumulation hypothesis*. In 1952, Medawar proposed that aging is caused by many harmful genes, accumulated over evolutionary time, that act late in life and, as the survivors are few at older ages, are insufficiently removed by natural selection.
- *Antagonistic pleiotropy hypothesis*. Aging is due to genes with multiple (pleiotropic) actions, i.e., genes that are beneficial in the young or adult stage but disadvantageous at later ages. Therefore, they are only partially eliminated by natural selection.
- *Disposable soma hypothesis*. Biochemical and physiological limits hamper the efficiency of the maintenance systems at older ages. So, in the evolutionary search of the best division of metabolic resources between reproduction and somatic maintenance, the first is preferred.

These "evolutionary" theories of aging show some common characteristics: (i) they consider only individual selection, and therefore aging is always considered as exclusively harmful and opposed by natural selection; and (ii) aging is always attributed to an insufficiency of natural selection or to conflicting evolutionary demands, and so natural selection is able only partially to counteract aging.

Moreover, these theories have in common with the non-evolutionary theories the following characteristics: (i) aging is the consequence of multiple harmful events that the organisms cannot counteract; and (ii) aging is not determined by specific mechanisms or genes, i.e., it cannot be defined as a genetically programmed phenomenon.

In 1961, Aldo Carl Leopold, a botanist, proposed that aging was adaptive because it increased the evolutionary ability of a species to modify its genes: "... in plants senescence is a catalyst for evolutionary adaptability" (Leopold 1961, p. 1729). Somehow Leopold followed the intuitions of Wallace and Weismann, again proposing that aging favors evolution because it accelerates generation turnover. Moreover, he clearly proposed that aging was due to specific mechanisms ("We can safely assume that there are some internal biological mechanisms which bring about decline in viability and increase in vulnerability in such populations" [Leopold 1961, p. 1727].), i.e., a clear definition of aging as an adaptive phenomenon, genetically determined and programmed.

Some years later, aging was proposed as beneficial in terms of supra-individual selection, through a kin selection mechanism, in populations divided into demes and demographically stable (Libertini 1988, 2006). Moreover, a paradoxical inverse relationship between extrinsic (or environmental) mortality and the proportion of deaths due to the age-related mortality increase was predicted by this theory (Libertini 1988), and later it was shown that the prediction was confirmed by empirical data (Libertini 2006).

The theory, proposed in 1988 (Libertini 1988), was posed again in more complex models of

populations similarly spatially structured (Travis 2004; Martins 2011; Mitteldorf and Martins 2014). In particular, it was also predicted the aforesaid inverse relationship and highlighted that it is a general prediction of programmed aging theories in contrast with the prediction of nonadaptive theories: "this complementary relationship between background death and evolved senescence is characteristic of adaptive theories of aging. A high background death rate leads to a *longer* evolved life span. This contrasts with classical theories, in which a high background death rate leads to a *shorter* evolved life span" (Mitteldorf and Martins 2014, p. 293). It is remarkable that, for this contradiction with nonadaptive aging theories, no explanation compatible with them has been attempted.

Another hypothesis proposed that aging was a form of defense against the spread of infective diseases (Mitteldorf and Pepper 2009). It was also proposed that in general, aging was favored by natural selection as it increases the evolvability, or the ability to evolve, of a species (Goldsmith 2008).

An important contribution was the definition of the concept of phenoptosis as "the programmed death of the body" (Skulachev 1997, p. 1191) and the subsequent definition of aging as a form of slow phenoptosis (Skulachev 2002). With this concept, regardless of the specific mechanisms that determine aging, it was pointed out that this phenomenon was genetically and adaptively determined, i.e., programmed. Moreover, the phenoptotic phenomena of which aging was an example were not a rare exception but, on the contrary, a large category of phenomena well known and documented and with an adaptive nature that was clear and undisputed (Finch 1990). Paradoxically, in the great set of phenoptotic phenomena, aging was perhaps unique in its characteristic of not being considered as adaptive (Libertini 2012).

General Classification of Aging Theories

Hypotheses, or theories, about aging can therefore be classified in two different ways that intertwine with one another. The first is obtained by dividing them into non-evolutionary and evolutionary theories: (i) the non-evolutionary hypotheses embrace all the theories prior to the proposal of the mutation accumulation theory, with the exceptions of the not well-defined intuitions of Wallace and Weismann previously mentioned; and (ii) evolutionary hypotheses embrace the theories from Medawar onward, with exceptions – not mentioned here – that in a more or less obvious way repeat ideas of the other group.

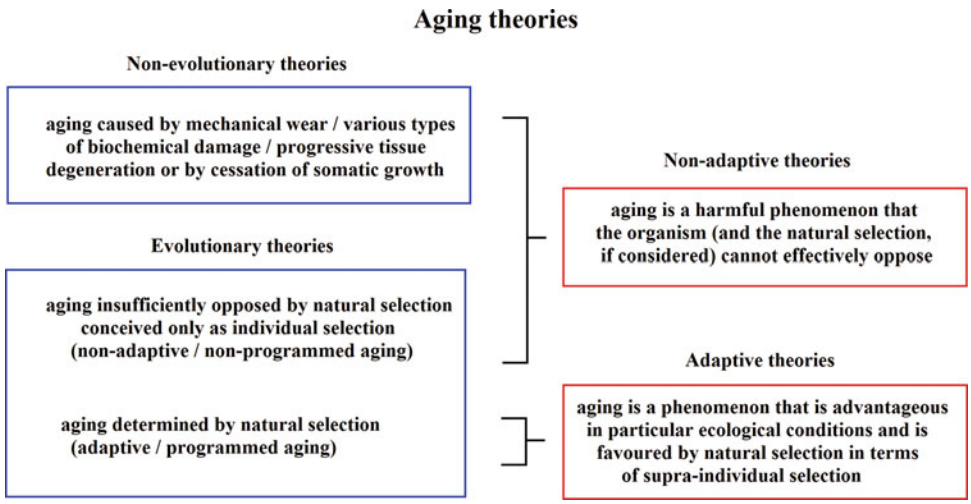
A different classification divides them into theories that interpret aging as a nonadaptive phenomenon ineffectively contrasted by natural selection and those that, on the contrary, explain aging as an adaptive phenomenon determined and modulated by the evolution because favored by natural selection at supra-individual level: (i) the first group includes all the non-evolutionary theories and many of the evolutionary theories, in particular the mutation accumulation hypothesis, the antagonostic Antagonistic pleiotropy hypothesis, and the disposable soma hypothesis; and (ii) the second group includes the theories mentioned above from Leopold's paper onward.

These subdivisions and their partial reciprocal overlapping are summarized in Fig. 1.

Aging Theories and Evidence

The theories of aging are very numerous. Medvedev in 1990 listed 300 hypotheses (Medvedev 1990), and the list is now certainly incomplete if we consider also the hypotheses proposed since then. This may lead us to believe that a truthful theory for aging is far and difficult to achieve. However, it must be considered that (i) various theories are based on overlapping concepts and can be treated in an overall way, (ii) theories that predict opposite things cannot be simultaneously true, and (iii) it is possible to evaluate the coherence of the predictions of each theory with the empirical data and with some theoretical arguments.

In fact, aging theories, despite their number, can be divided into six theories or groups of theories, of which two are non-evolutionary, damage



Non-evolutionary and Evolutionary Aging Theories, Fig. 1 Scheme of classification of the types of aging theories

Non-evolutionary and Evolutionary Aging Theories, Table 1 Correspondence between empirical data/theoretical arguments and the various theories. (From Libertini 2015, modified)

Empirical data or theoretical arguments	DA	CSG	MA	AP	DS	AA
1. Non-universality of aging	No/–	Yes	No/–	No/–	No/–	Yes
2. Great interspecific variation of aging rates	No/–	Yes	No/–	No/–	No/–	Yes
3. Effects of caloric restriction on life span	–	–	–	–	No	Yes
4. Damage of aging for the senescing individual but its advantage in terms of supra-individual selection	No	–	No	No	No	Yes
5. Existence of fitness decline in wild conditions	No	Yes	No	No	No	Yes
6. Proportion of deaths due to intrinsic mortality inversely proportional to extrinsic mortality, in a comparison of species	No	No	No	No	No	Yes
7. Impossibility of explaining age-related fitness decline as a consequence of genes that are harmful at a certain age	–	–	No	–	–	Yes
8. Age-related progressive decline of cell turnover capacities	No	No	No	No	No	Yes
9. Cell senescence	No	No	No	No	No	Yes
10. Gradual cell senescence	No	No	No	No	No	Yes

Abbreviations: No, not explained or predicted by the hypothesis or in contrast with its predictions; Yes, predicted by the hypothesis or compatible with it; –, irrelevant for accepting/rejecting the hypothesis

accumulations hypotheses (DA) and cessation of somatic growth hypothesis (CSG), and four evolutionary, mutation accumulation hypothesis (MA), antagonistic pleiotropy hypothesis (AP), disposable soma hypothesis (DS), and adaptive aging hypotheses.

A paper (Libertini 2015) has investigated the correspondence between the predictions of these theories and empirical data or some theoretical arguments. The results, summarized in Table 1, show that adaptive hypotheses are in complete accordance with empirical data or theoretical arguments, while the other theories are in serious (CSG) or total contrast (DA, MA, AP, DS).

Summary

The existence of hundreds of aging theories indicates that certainly most of what they propose is contradictory and erroneous. The main criteria for reducing the size of this tangle of hypotheses

should be (i) compatibility of each of them with the mechanisms of natural selection and (ii) compatibility of the predictions deriving from each hypothesis with the data obtained from empirical evidence. An analysis conducted with these criteria shows that evolutionary aging theories proposing an adaptive value for aging are largely the most plausible hypotheses.

Cross-References

- Aging as Phenoptotic Phenomenon
- Aging Definition
- Antagonistic Pleiotropy Aging Theory
- Cessation of Somatic Growth Aging Theory
- Disposable Soma Aging Theory
- Evolvability Aging Theory
- Kin Selection Aging Theory
- Mitochondrial ROS Aging Theory
- Mutation Accumulation Aging Theory
- Non-programmed (Non-adaptive) Aging Theories
- Oxidation Damage Accumulation Aging Theory
- Programmed (Adaptive) Aging Theories
- Timeline of Aging Research

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