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Programmed (Adaptive) Aging Theories

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Synonyms

Adaptive aging theories; Programmed aging theories

Definition

Programmed or adaptive aging theory is based on the thesis that aging, described as age-related increasing mortality, is a physiologic function. This interpretation implies that aging is adaptive, i.e., favored by natural selection (in terms of supra-individual natural selection), and programmed, i.e., genetically determined and modulated. This definition is opposed to that of non-programmed or nonadaptive aging theories that explain aging as the result of many degenerative phenomena insufficiently countered by natural selection and without any adaptive meaning or specific programmed mechanism.

Overview

Anything deteriorates and wears over time. The age-related decline of the functions of living beings appears to be a clear example of this general decline of everything. This explains well why aging is traditionally explained as an inevitable phenomenon due to the gradual accumulation of the effects of noxious metabolic substances, wear and tear of every organ and tissue, and harmful outcomes of many factors. In this interpretation of aging (nonadaptive or non-programmed paradigm), the phenomenon is not determined or regulated by specific genes, is not an adaptation for a function, and is countered by natural selection that manages to curb its manifestations with varying effectiveness depending on the species.

The opposite interpretation (adaptive or programmed aging paradigm) maintains that aging has an evolutionary advantage and is therefore determined and modulated by specific genes favored by natural selection, and for many scholars appears as an untenable idea, without any ground and to be surely discarded. For a very long time the concept that aging could be somehow advantageous was excluded by everyone, apart from some sporadic and undocumented statement that aging could be useful as it frees up space for the younger generations and thus allows the spread of new favorable genes (Weismann 1889).

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Questions About Programmed Aging Theories

It is useful to highlight the concepts (below, *in italics*) underlying the constant and strong exclusion of the possibility that aging could be adaptive and also which arguments make such ideas unsustainable (below, not in italics):

(i) *By universal and unquestioned physical law, entropy, i.e., the degree of disorder of any system, always increases with time, and this would make the greatest disorder that characterizes senile age inevitable* (Hayflick 2007).

However, this law refers to a closed system, and if energy is given to the system by external sources, entropy may also decrease. Living organisms are examples of open systems that take energy from the outside (photosynthetic organisms from light, organisms that feed on plants or other living beings from their energies), and so the increase of entropy is not inevitable in a living being.

(ii) *The main law of evolutionism is that natural selection favors characters that allow a greater capacity for survival and reproduction. As aging compromises both survival and reproduction capacities, it is impossible that this phenomenon can be favored by natural selection*.

A famous simplification of the concept of natural selection, "the survival of the fittest," i.e., by using modern terminology, the spreading of genes of those individuals who are fittest to survive and reproduce, was proposed by Spencer (Spencer 1864) and only later was adopted by Darwin ("Natural Selection or the Survival of the Fittest" (Darwin 1869)).

Indeed this concept is true for selection at the individual level but the same is not true for selection at the supra-individual level: the same Darwin did not exclude that some characters even if deleterious for the individual might be favored because useful for the group (Darwin 1871). The kin selection (Hamilton 1964; Trivers 1971), a big advance in evolutionary studies, explained how characters that are harmful to the individual but advantageous to genetically related individuals may be favored by natural selection. The kin selection is not something opposite to individual selection. In effect, let us suppose that a gene C determines effects not only on the individuals I_1, where C exists, but also in other individuals $I_2, I_3, \ldots I_n$, related with I_1, i.e., where there is a probability that C is in the genome of I_x equal to the coefficient of kinship between I_x and I_1 (r_x). With these conditions, and with S_x indicating the effects of C on the fitness of I_x and P_x the reproductive capacity of I_x, C will be favored by natural selection when:

$$\sum_{x=1}^{n} (S_x \cdot P_x \cdot r_x) > 0 \qquad (1)$$

Clearly, when n=1, as r_1=1, the Formula (1) becomes:

$$S \cdot P > 0, \qquad (2)$$

that well describes the individual selection. Therefore, the individual selection is only a particular case of kin selection (Libertini et al. 2017).

Formulas describing certain cases of group selection can be derived from the same Formula (1) (Libertini et al. 2017). This means that, by using the argument that that fitness decline is harmful for the individual, it is wrong to exclude a priori the possibility that aging is favored by natural selection.

(iii) *If aging were determined by specific genes, we would have the paradox that natural selection favors genes that determine the death of the individual, an idea that appears to be untenable.*

Consistent with the arguments of the previous section, there is a very varied and common category of self-injurious phenomena, known for a long time and widely recognized as genetically determined (Finch

1990), which only recently has been defined with the unifying term of phenoptosis (programmed death of an individual) (Skulachev 1997). In such phenomena, certainly the result of mechanisms determined and regulated by genes, an individual causes its death or that of closely related individuals (Libertini 2012). In the study of phenoptotic phenomena, in their general and undisputed interpretation as adaptive phenomena, aging represents a singular exception as it is interpreted mostly as nonadaptive.

(iv) *Under natural conditions, old individuals are rare or absent. Even if one wants to admit that aging is in some way adaptive, natural selection cannot act on old individuals, due to their rarity or absence in the wild, and therefore an adaptive value for aging would be impossible.*

This idea originates from the confusion between the concept of aging (progressive age-related decline in fitness) and that of aged individuals (individuals with clear and strong manifestations of aging): "As a rule, wild animals simply do not live long enough to grow old. Therefore, natural selection has limited opportunity to exert a direct influence over the process of senescence" (Kirkwood and Austad 2000, p. 233). On the contrary, it is well known that the decline of fitness is present and well documented in natural conditions (Libertini 1988; Ricklefs 1998; Nussey et al. 2013). In particular: "The recent emergence of long-term field studies presents irrefutable evidence that senescence is commonly detected in nature. We found such evidence in 175 different animal species from 340 separate studies" (Nussey et al. 2013, p. 214).

(v) *All species show the phenomenon of aging. This proves that aging is inevitable for living beings and that there is no need for a specific program that determines senescence.*

Old individuals of many species, which are defined as species with negligible senescence, show no signs of aging (i.e., increasing mortality/declining fitness) under natural conditions (Finch 1990; Dahlgren et al. 2016; Jones and Vaupel 2017). For them, mortality rate is constant at every age that is present in natural conditions and the duration of life is determined by causes of death that exist at all ages.

Moreover, most species have particular life cycles different from aging, here precisely defined as age-related mortality increase (e.g., reproduction followed by rapid death) (Finch 1990; Jones et al. 2014). These different life cycles are clearly genetically determined or programmed (Jones et al. 2014). If aging as before defined was not determined by a program, it would be an unusual and perhaps unique example of life table not determined by a program.

(vi) *If aging is adaptive, the existence of specific mechanisms that determine and regulate the progressive decline of fitness is indispensable, but these mechanisms are unknown and unlikely to exist: "No genetic instructions are required to age animals, just as no instructions on how to age inanimate machines are included in their blueprints . . . there are no genes directly responsible for the processes of aging"* (Olshansky et al. 2002, p. B294).

On the contrary, these mechanisms exist and are well known. They are based on the *Telomere-subtelomere-telomerase system* (see the entry) and are the subject of countless studies that cannot be summarized here for the sake of brevity. These mechanisms cause the progressive reduction of cell duplication capacity, the decline of cellular functions (see the entry *Gradual cell senescence*), the slowing of cell turnover, and the overall decline in fitness.

The Birth of Programmed Aging Thesis

Despite these ideas that have been and are a huge obstacle for the acceptance of the possibility that aging is an adaptive phenomenon and therefore determined by specific genes, after an incredibly long pause that followed the sterile intuitions aforementioned of Wallace and Weismann,

finally, in relatively recent years, some works were published that supported this daring thesis.

In 1961, a botanist proposed the adaptive nature of aging, suggesting the evolutionary advantage deriving from the quick succession of generations, and the existence of mechanisms that determine aging: "This type of survivorship [i.e., an age-related increasing mortality after a certain age] is common to many animals, and again probably to many perennials plants. We can safely assume that there are some internal biological mechanisms which bring about decline in viability and increase in vulnerability in such populations. . . . Another effect of senescence of positive value may be its impact on natural selection and hence on evolutionary change. With the long life span of perennial plant species, there is a buffering against rapid evolutionary change. If a species of plant were to exist which did not senesce at all and which was subject to limited mortality, the original population would linger on and on, continuing to reproduce its original genome, and the evolutionary ability of this species to adapt to new environmental changes would be minimal. I assert, then, that in plants senescence is a catalyst for evolutionary adaptability" (Leopold 1961, p. 1727).

In 1988, also inspired by Leopold's work, a theory was proposed that attributed to aging a positive value in terms of supra-individual selection. According to this hypothesis, aging was favored by a mechanism based on kin selection if there was the ecological condition of the division of the species into demographically stable demes (Libertini 1988).

The subsequent works that were published in support of the idea that aging is an adaptive phenomenon are summarized in the entry *Non-evolutionary and evolutionary aging theories* and for the sake of brevity are not repeated here.

However, it is useful to underline that: "if aging is a function, i.e. a physiological program that is genetically determined and regulated, and provided that aging mechanisms are sufficiently known, it should be possible to conceive possible modifications of this program that could hamper or even cancel age-related fitness decline. In contrast, this is not at all likely if, as proposed by the old paradigm [i.e., non-programmed aging theories], aging is an inevitable consequence of the cumulative effect of various damaging factors that act on many cellular and organismal processes" (Libertini and Ferrara 2016, p. 1413).

Conclusion

The interpretation of aging as an adaptive and therefore genetically regulated phenomenon, as well as being of considerable importance both in evolutionism and in the whole of biology, is the theoretical basis for the ambitious idea of possible modifications of the aging process even to the point of reaching the condition of those species with negligible senescence.

This possibility is totally denied by the opposite nonadaptive interpretation of aging: "Although it is possible to reduce the risk of aging-related diseases and to mask the signs of aging, it is not possible for individuals to grow younger. This would require reversing the degradation of molecular integrity that is one of the hallmarks of aging in both animate and inanimate objects. Other than performing the impossible feat of replacing all of the cells, tissues, or organs in biological material as a means of circumventing aging processes, growing younger is a phenomenon that is currently not possible" (Olshansky et al. 2002, p. B294).

As for the predictable ethical or philosophical or religious or social objections related to this possible aim, they are certainly extremely important but not within the limits of science (Libertini 2009; Libertini and Ferrara 2016) and are not discussed here.

Cross-References

- ▶ Evolvability Aging Theory
- ▶ Kin Selection Aging Theory
- ▶ Non-Evolutionary and Evolutionary Aging Theories
- ▶ Timeline of Aging Research

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