Aging as an Evolved Characteristic – Weismann's Theory Reconsidered

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Summary Theories of aging have become significantly more important because of discoveries which indicate that aging is not universal or inevitable and which therefore indicate that major medical intervention in aging is possible. Directions of anti-aging research could be significantly influenced by basic theories of aging. Weismann proposed in 1882 that aging was an evolved genetically programmed adaptation that had a species benefit. Since then this idea has been largely replaced by various theories in which aging is not an adaptation but results from accumulated adverse mutations or is an adverse side effect of some essential process. Arguments are presented to the effect that aging is an evolved beneficial characteristic and is therefore likely to result from a more complex and structured mechanism than if it resulted from more random processes such as mutation accumulation. Further, aging appears to be one of a number of related and interactive life-cycle characteristics including age-at-puberty suggesting that it might be controlled by similar biological mechanisms.

"One seldom errs by overestimating the complexity of a biological process". -Anonymous

INTRODUCTION

Prior to Darwin (~1850), there was little reason to distinguish between longevity and any other characteristic of a particular animal species. Whatever caused a rat to have bulbous eyes and a long tail presumably also caused it to have a certain life span, which, like eyes and tail, varied between individuals and species and seemed to fit with other characteristics of animals as part of a logical design.

However, Darwin's theory of natural selection(1) required that any evolved trait benefit the survival and reproductive fitness of an organism. Since aging was deleterious to fitness, and longevity was indefinitely beneficial, it was immediately apparent that observed longevity and aging did not fit the rules of natural selection for an evolved characteristic. Although Darwin continued to believe that longevity was an evolved trait, and believed that a limited life span was of benefit to some species, he did not suggest a mechanism whereby a trait that was adverse to fitness could evolve or propose a specific benefit for aging.

Weismann(2) (~1882) proposed that "programmed death" was an evolved characteristic which had a specific species benefit in that it freed resources for younger, more adapted, members of the population. Weismann's hypothesis has been largely rejected because of two problems:

First, no mechanism was specified which would allow evolution of a "species benefiting" characteristic which had a negative effect on fitness. Many believed (and continue to believe) that any possible species benefit would be overridden by a fitness disadvantage. The mechanics surrounding evolution of a species benefit did not appear to be workable: Would a species have to become extinct (or not) in order to "express" a species disadvantage or benefit? The evolution of a species benefit, if possible at all, was seen as "slow" relative to a fitness benefit.

Second, the specific characteristic proposed by Weismann was "programmed death". Since very few animals under wild conditions live long enough to "die of old age", many felt that programmed death could not have been expressed in any significant number of organisms and could therefore not have been a result of natural selection.

Subsequent to the failure of Weismann's hypothesis, theorists concentrated on hypotheses in which aging is not an evolved adaptation but is the result of a more random process. However, simple, "accumulation of damage" theories were unable to explain the wide disparity in longevity observed between different species. In 1952 Medawar advanced the mutation accumulation theory(3) in which aging is the result of the accumulation of random, late acting, adverse mutations which affect animals only relatively late in life, therefore have only a minor effect on fitness, and are therefore only weakly selected against. There are a number of similar, currently respected, theories including the antagonistic pleiotropy theory(4). Because the age at which out-selection pressure becomes less significant is presumed to be related to the age of sexual maturity, these theories provided a better fit to the inter-species disparity in aging. Traditional, non-adaptive theories tend to be very pessimistic regarding major medical intervention in aging because aging is seen as an unavoidable side effect of an essential process or a defect so intractable that evolution has been unable to find a solution.

Theories of aging have recently become significantly more important because the discovery of species having negligible aging(5,6) and the discovery of aging genes(7) as well as continuing investigations into the life span extending effects of caloric restriction(8) have made it clear that there is a real possibility for development of major anti-aging treatments. Some discoveries such as aging genes seem to be incompatible with some of the non-adaptive theories. Directions of research into the mechanics of aging and anti-aging treatment could be significantly influenced by basic theories of aging.

This article suggests some potential solutions to the problems with Weismann's theory.

FITNESS AND EVOLUTIONARY CAPACITY

Darwin's theory assumes that all organisms have the ability to evolve, that is, the ability to adapt to changes in their world through natural selection, and that this *evolutionary capacity* or *evolvability* is a constant property of life that cannot be affected by any evolved trait. The natural selection theory also holds that natural variation in characteristics between individuals in the population of a species is an essential component of this constant evolvability.

Subsequent discoveries in genetics have disclosed that variation in more advanced organisms is actually largely the result of complex and obviously evolved mechanisms such as sexual reproduction, meiosis, and gene crossover and that therefore the ability to adapt by means of variation and natural selection varies between different organisms and can be affected by evolved characteristics. Simpler organisms with more clonal methods of reproduction have a lesser degree and quality of variation. Variation as an evolved characteristic is itself incompatible with natural selection theory because organisms with a larger degree of variation are, on average, less fit than organisms with lesser variation. If, for example, a certain height is optimum, then animals that are either less or more than the optimum height are less fit. Similarly, genetic diversity favors evolutionary capacity at the expense of fitness. Many other characteristics of animals including life span plausibly affect evolvability. An organism with greater evolvability would have a competitive advantage in that it would be able to adapt more rapidly than a competing organism. These issues have led to development of a recent (~1989) branch of evolutionary theory (evolvability theory(9, 10)).

It appears that most if not all characteristics which positively affect evolutionary capacity (such as variation) negatively affect fitness and that therefore any species capable of further adaptation represents a compromise or tradeoff between fitness and evolutionary capacity. A characteristic that increases evolutionary capacity can therefore reduce fitness and still be an evolved characteristic. Fitness favors current organisms as seen from any particular point in time. Evolutionary capacity favors future organisms at the expense of current organisms. Since mammals are at the end of a very long chain of evolution, it is apparent that throughout that chain of descendency a non-zero evolutionary capacity must have existed.

The degree to which a species "needs" evolutionary capacity varies. Species such as mammals which are confronted by rapidly evolving predators or prey would have a higher requirement for evolutionary capacity than species with a more static world.

ADULT DEATH RATE AND EVOLUTIONARY CAPACITY

Natural selection functions through the statistical differential in life spans between fit and less fit organisms. It is therefore apparent that death rate must be a factor in evolutionary capacity. A hypothetical animal that did not die could not evolve. Darwin proposed that each successive generation of an evolving species is minutely better adapted. If so, organisms with a shorter life span have a competitive advantage over otherwise originally identical organisms with a longer life span because they can accumulate these incremental improvements in adaptation more rapidly. Conversely, it is also apparent that in order to be selected, a trait must be expressed in such a way that it affects the probability of survival. Deaths of immature organisms that occur prior to expression of an adult characteristic cannot contribute to selection of that characteristic. (Recall that this was an issue with Weismann's hypothesis.) Therefore, *adult death rate* is a factor in the ability to evolve adult characteristics. The optimum life span for an animal would therefore appear to include a period in which the animal develops adult characteristics followed by a period in which natural selection would operate.

Although Darwin considered that the growth of animal populations was "checked" by external conditions (predators, food supply, etc.), mammals also have many internal characteristics which act as restraints on reproduction such as age-at-puberty, frequency and length of fertile periods, litter size, gestation period, mating rituals, and aging. Although most of these "life cycle" characteristics have some fitness purpose, as a group they act to influence adult death rate and therefore also have an evolutionary capacity component.

Maximizing adult death rate would appear to result from optimizing the combined effect of external conditions and internal life cycle characteristics. If we consider a hypothetical optimized mammal and alter its puberty age to be lower, younger animals would begin reproducing. Population pressure would then cause a reduction in median life span, reducing adult death rate. If we instead decrease the aggressiveness of the animal's aging mechanism, some animals would begin reproducing at older ages, thus again increasing population pressure and decreasing median life span and adult death rate. Life cycle characteristics, especially puberty age and aging appear to be among the most superficial and flexible of animal characteristics in that they vary greatly between even similar species. This flexibility could allow the animals to maintain a high adult death rate and thereby maximize their evolvability under different external conditions. This sort of advantage could also explain the observed relationships between food supply and reproduction and aging(8), in which internal life cycle characteristics appear to vary in response to external conditions.

Evidence of such adaptation suggests a complex evolved mechanism. Stress causes beneficial effects on bone density, muscle mass, and angiogenesis but why would a condition caused by a random adverse mutation be beneficially affected by stress in the form of caloric restriction?

EFFECTS OF AGING

Under wild conditions, animals die of predator attack, attack by members of the same species (warfare), inability to obtain food or water, disease, accident, or adverse environmental conditions. Aging in mammals causes gradually increasing weakness, loss of mobility, and increased susceptibility to disease and environmental conditions and therefore, (not coincidently), increases the probability of death from all of the causes listed above. The probability of an animal dying in any given time period (proportional to death rate) therefore declines as it matures, reaches a minimum and then increases. Because even a relatively minute deterioration will cause a statistically significant increase in death rate, one suspects that the evolutionary effects of aging in wild mammals begin at relatively young ages. Observed death rates in wild mammals increase beginning at puberty(11). The expressed effects of aging in wild populations are therefore significant.

It is assumed for purposes of this discussion that decline of reproductive capability and vigor is also part of the aging process. The probability that a surviving animal will breed in any given time period therefore increases after sexual maturity, reaches a maximum, and then declines.

EVOLUTIONARY CHALLENGE

The highly structured and obviously evolved mating rituals observed in many animals have a *challenge effect* which increases evolutionary capacity by increasing the differential in breeding rate between fit and less fit animals. An animal, which has superior strength, stamina, or other beneficial trait can overcome the challenge presented by the mating ritual and breed or breed at a *younger* age than an animal without such traits.

Mating rituals have the general effect of (on average) delaying mating in a population sensitive way. In larger populations, the delay due to the mating ritual would tend to be greater because the number of competing animals would be greater and animals would need to be more mature to successfully compete. Because of the delay, generic natural selection has a longer period in which to operate. The animals that survive long enough to mate therefore presumably exhibit more beneficial characteristics than they would without the mating ritual. These animals are also more likely to fully express adult characteristics.

Aging has a very similar and complementary challenge effect. An animal with beneficial traits can overcome the gradually increasing deleterious effects of aging to survive, pass a mating ritual, and breed to an *older* age than an animal without such traits. Skulachev(12) suggested in 1997 that aging was an evolved adaptation in which the appearance of a useful trait allows compensation of the effect of aging within certain time limits.

Some mating rituals (e.g. *Ovis Canadensis* (Bighorn Sheep)) clearly have a greater negative effect on fitness than aging.

NEGATIVE EVOLUTIONARY EFFECTS OF IMMORTALITY

Weisman proposed that in the absence of aging, older and less evolved animals would compete for resources with younger, presumably more adapted animals, thus detracting from evolution.

If we compare the performance of a hypothetical non-aging mammal with the aging version of the same mammal, we would expect to see the following additional negative effects on evolutionary capacity in the non-aging animals.

The non-aging animal does not undergo deterioration in physical or reproductive capability upon attaining maturity. We would therefore expect the death rate for such animals to be nominally constant once becoming adult instead of increasing with age as observed in aging animals. The rate at which such animals would produce young would also be constant instead of decreasing with age. The number of animals of a given age in the adult population would decline with age at an exponential rate determined by the animal's situation regarding predators and other causes of death but the average number of young produced by each animal would be proportional to age. This would lead to a situation in which a relatively small (relative to the aging case) number of animals would produce the majority of the young so that the genetic diversity in the non-aging population would be significantly less than in the aging population, an evolutionary disadvantage.

Two additional factors make this situation in the non-aging group more severe. First, mammals have intelligence and therefore learn from experience. Older animals will therefore be more capable of dealing with predators, competitors, food acquisition, and environment than younger animals. Death rates in non-aging animals would therefore be expected to *decline* with age and breeding rates would be expected to *increase* with age. Similarly, animals which survive infectious diseases would obtain some immunity against subsequent infection. Therefore the older a non-aging animal became, the less likely it is to die of an infectious disease. These factors further reduce genetic diversity in a non-aging population.

Finally, a non-aging population would have disadvantages regarding adult death rate and challenge effect as described above.

Absence of aging seems particularly incompatible with the reproductive habits of some mammals. Consider how absence of aging would affect genetic diversity in a population in which reproduction is essentially limited to *older, more experienced* males.

ANTI-AGING RESEARCH IMPLICATIONS

The traditional and prevailing view that aging is *not* an evolved, genetically programmed, characteristic is based on 150-year-old evolutionary theory that is increasingly seen as incomplete. The often-heard assertion that aging *cannot be* an evolved trait is based on the presumption that "The Theory" is so perfectly complete, comprehensive, and all encompassing, that any exceptions, modifications, or extensions (such as suggested here) are impossible. Even Darwin did not take that view.

An informal survey(13) indicates that about 80 percent of the population believes that major medical intervention in the aging process is impossible or very unlikely, an attitude with an obvious chilling effect on the funding and staffing of anti-aging research. If aging *is* an evolved characteristic as suggested here, prospects and methodology in anti-aging research would be significantly affected because an evolved aging mechanism would be expected to be much more complex than one resulting from more random processes thus offering additional points at which medical intervention could be applied. If, in addition, aging is one of a family of highly related and interactive life cycle characteristics, it is reasonable to believe that aging is very centrally controlled in a manner similar to that of other life cycle characteristics such as puberty age with mechanisms that similarly involve complex hormone control chains. (Kenyon(14) reports finding hormone mediated aging in C. *elegans*.) Aging may in fact be part of a larger evolved mechanism that controls many life cycle characteristics.

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