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Review

Evolution of lifespan

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HIGHLIGTHS

- Lifespan extension is a primary mode of evolution.
- Lifespan extension results in a larger body/brain and advanced behaviour.
- Lifespan extension has mediated hominin evolution.
- Lifespan extension could equate with macroevolution.
- Lifespan extension represents major internal mediation in evolution.

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ABSTRACT

Present day evolutionary theory, modern synthesis and evo-devo, appear to explain evolution. There remains however several points of contention. These include; biological time; direction; macroevolution verses microevolution; ageing and the extent of internal as opposed to external mediation. A new theoretical model for the control of biological time in vertebrates/bilaterians is introduced. Rather than biological time being controlled solely by a molecular cascade domino effect it is suggested there is also an intracellular oscillatory clock. This clock (life's timekeeper) is synchronised across all cells and runs at a constant frequency throughout life. Slower frequencies extend lifespan, increase body/brain size and advance behaviour. They also create a time void which could aid additional evolutionary change. Faster frequencies shorten lifespan, reduce body/brain size and diminish behaviour. They are therefore less likely to mediate evolution in vertebrates/mammals. It is concluded that in vertebrates, especially mammals, there is a direction in evolution towards longer lifespan/advanced behaviour. Lifespan extension could equate with macroevolution and subsequent modifications with microevolution. As life's timekeeper controls the rate of ageing it constitutes a new genetic theory of ageing. Finally as lifespan extension is internally mediated this suggests a major role for internal mediation in evolution.

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1. Introduction

The contention that evolution is mediated by natural selection originated from the publication 'On the Origin of Species by Means of Natural Selection' by Darwin (1859). Darwin's theory suggested the environment, rather than intelligent design (Paley, 1802; Bell, 1833; Ayala, 2007), as the mediator of different species. The theory envisaged evolution occurring in small gradual internally mediated steps, shaped and directed by the environment. With the advent of population genetics in the 1930s internal change was demonstrated to be random, non-directional and occurring in small steps. This was fully compatible with Darwin's theory and the evolutionary model, combining natural selection and population genetics, became known as the modern synthesis or neo-Darwinism. The modern synthesis has been supplemented in more recent years with evolutionary developmental biology (evo-devo), providing a greater understanding of the role of development in evolution (Raff, 2000). Rather than genes in general evo-devo emphasises the importance of change to key developmental regulatory genes. Change in these genes can result in a faster pace of evolution, hence makes it more compatible with evidence for this in the fossil record. Present day evolutionary theory therefore represents a combination of the modern synthesis and evo-devo (Gilbert, 2003). This present day view of evolution is still considered to be entirely compatible with Darwin's theory of natural selection. There has however been some de-emphasis on gradualism. It is now accepted that internal change can occur in slightly larger steps than was envisaged in the modern synthesis. This permits, at least to some extent, a faster pace of evolution.

This review, focusing on vertebrates and possibly all bilaterians, suggests a new dimension to present day evolutionary theory. The new dimension relates to lifespan and its role in evolution. It has been hypothesised that a free running intracellular oscillatory clock, running at a constant frequency, splits lifespan into equal length phases (Neill, 2013). Phase length is determined by the frequency of the oscillations, with one oscillatory cycle representing one phase. This clock, named life's timekeeper (LT), is synchronised across all cells. The frequency of LT is species specific. A slower frequency leads to longer life phases and hence a longer lifespan, with a faster frequency mediating shorter phases and lifespan. The number of phases involved in maturation is considered to remain relatively constant, at least within individual lineages. Within lineages total maturational time is hence determined by the length of phases rather than number of phases. Alterations in the frequency of LT, especially slower frequencies, have been proposed to have mediated evolutionary change. Assuming that cell cycle time is independent of LT frequency then a significant change to its frequency can result in change to size, morphology, behaviour and lifespan. This magnitude of internal mediated change, which could occur over relatively few steps, is considerably greater than presently envisaged in evolutionary theory. As such if the concept of LT turns out to be correct then it would change present day evolutionary theory, with regards to vertebrates and possibly all bilaterians, towards a greater level of internal mediation. Although natural selection undoubtedly remains important its role as the sole/dominant mediator of vertebrate/bilaterian evolution could be questioned.

2. Evolutionary theory

2.1. Modern synthesis and evo-devo

The modern evolutionary synthesis or neo-darwinism originated in the 1930s and 1940s (Fisher, 1930; Wright, 1931; Dobzhansky, 1937; Mayr, 1942; Simpson, 1944). It resulted from an amalgamation of Darwin's theory of natural selection with genetics. Evolution was seen as a gradual process, occurring through accumulative small step allele frequency deviations between populations. The allele deviations resulted from genetic drift, recombination and mutation. Speciation was proposed to be mediated through some degree of reproductive isolation. Although geographical isolation was often involved complete geographical isolation was not necessary. This theory was proposed to explain evolution over short (microevolution) and long time periods (macroevolution). Macroevolution was in effect repeated rounds of microevolution.

Although embryology played an important part in evolutionary theory prior to the modern synthesis it was generally ignored in the modern synthesis. A re-awakening of the role of embryology/development in evolution originated in the work of Goldschmidt (1940), Waddington (1953), also see Dietrich (2003), Hall (1992), Slack (2002). They questioned the ability of the modern synthesis to fully explain macroevolution, suggesting a role for development. The modern synthesis was also questioned by palaeontologists as its emphasis on gradual change seemed inconsistent with evidence for periods of stasis and rapid change in the fossil record (Eldredge and Gould, 1972).

The advent of modern day evo-devo was in the 1980s. This followed several important publications, together with increasing advances in understanding developmental genetics at the molecular level. One of the most influential publications was 'Ontogeny and Phylogeny' by Gould (1977a). Other important publications included 'Embryos, Genes and Evolution: The Developmental-Genetic Basis of Evolutionary Change' (Raff and Kauffman, 1983) and 'Evolution by Tinkering' (Jacob, 1977). An important advance in molecular genetics was the demonstration that human and chimpanzee genes were over 99% identical (King and Wilson, 1975).

It is now evident that there is much less variation in genes throughout the animal kingdom than previously assumed. There appears to be a conserved bilaterian developmental toolkit with many developmental genes serving similar functions across all bilaterians (Erwin and Davidson, 2002; Erwin, 2009). Examples are the role of *pax*6 in eye development and the *hox* genes in determination of the anterior posterior axis (Lewis, 1978; McGinnis et al., 1984; Gehring, 1985, 2002). Rather than changes in genes it is now known that evolution can be mediated by changes in gene expression across time and space. The study of gene expression has highlighted the importance of cis-regulatory elements (CRE) (Prud'homme et al., 2007; Wray, 2007; Carroll, 2008). CRE are short DNA sequences upstream of genes that control gene expression through binding transcription factors. Each CRE can bind multiple transcription factors and each transcription factor binds to multiple CRE. Gene expression has therefore become visualised in relation to gene regulatory networks (GRN), depicting the interactions between all transcription factors

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