Dose-Response:
An International Journal
April-June 2019:1-4

DOI: 10.1177/1559325819843376
journals.sagepub.com/home/dos
SAGE

Hormesis Promotes Evolutionary Change

David Costantini[1]

Abstract

Exposure to moderate environmental stress is one important source of evolutionary change. This evidence would support the hypothesis that hormesis is an evolutionary expectation. In this short review, I discuss relevant examples of genetic and phenotypic responses to moderate stress exposure that are compatible *with hormesis and* with paradigms of evolutionary theory such as evolutionary rescue or phenotypic plasticity. Genetic recombination, nonlethal mutations, activity of transposable elements, or gene expression are some of the molecular mechanisms through which hormesis *might enable* organisms to maintain or even increase evolutionary fitness in stressful environments. These mechanisms span the tree of life from plants to vertebrates.

Keywords

epigenetics, evolutionary rescue, life history, phenotypic plasticity, recombination, stress

Introduction

Environmental stress has been one key driving force of evolution. It has long been recognized by evolutionary biologists that exposure to moderate amounts of stress may facilitate adaptation by inducing a number of genetic and phenotypic responses.[1-4] This pillar of evolutionary theory has not been so influential in other disciplines, such as those dealing with toxicology and environmental health risk assessment, where a less holistic view has traditionally predominated.

Dose–response models are one example of conceptual simplification of the biological reality, somehow needed to make such models operational. Dose–response models are actually used in environmental health risk assessment to predict the biological effects due to exposure to given environmental stressors or contaminants. The linear no-threshold (LNT) risk model is the current human health risk assessment paradigm. It simplistically assumes that the risk of adverse biological effects on the organism increases linearly, as the total dose of a natural or anthropogenic stressor (eg, contaminant, ionizing radiation, and ambient temperature) increases. In contrast, the hormetic model proposes that exposure to low or mild doses of environmental stress would have stimulatory rather than toxic effects on the organism, potentially increasing chances to survive and reproduce.[5-9] In other words, hormesis-based dose–response models capture a bit more of the biological complexity that the classic LNT models dramatically neglect. Prior work has, however, suggested that hormesis cannot be an evolutionary expectation because, while hormesis of certain aspects of individual performance may be possible, hormesis for fitness, itself, is not.[10] This is because short-term adjustments in any life-history trait (eg, in response to exposure to toxic agents) are expected to result in trade-offs with other fitness-related components.[10] Although this scenario is certainly plausible, there is a growing number of instances suggesting a significant role of hormesis in promoting evolutionary responses. Thus, there are conditions whereby hormetic mechanisms boost fitness to some degree or buffer it against any detrimental effects, indicating that hormesis may provide selective advantages.

In this short review article, my goal is to illustrate examples of key genetic and phenotypic responses of organisms to environmental stress that are compatible with expectations of hormesis and of evolutionary theory. To this end, I discuss relevant examples of experiments that support the role of hormesis in promoting both genetic and phenotypic responses of organisms to some environmental stressors. Although our understanding of the environmental conditions under which hormesis promotes adaptation is still elusive, the available evidence suggests that hormesis can be an evolutionary expectation.

[1] UMR 7221 CNRS/MNHN, Muséum National d'Histoire Naturelle, Sorbonne Universités, Paris, France

Received 26 November 2018; received revised 07 March 2019; accepted 20 March 2019

Corresponding Author:
David Costantini, UMR 7221 CNRS/MNHN, Muséum National d'Histoire Naturelle, Sorbonne Universités, 7 rue Cuvier, Paris, France.
Email: david.costantini@mnhn.fr

Brief Excursus to Evolutionary Thinking

In this paragraph, I have listed some processes that are thought to be fundamental in driving evolution.[4,11-15] Current theory sees evolution as a process by which allele (or genetic variants) frequencies change in a population over time. Genetic variation can arise from genetic recombination or gene mutations in response to environmental stressors. Some of these genetic responses are typical of evolutionary rescue, that is, those genetic changes that enable populations to respond to environmental perturbations irrespective of other factors such as gene flow, migration, or dispersal.[4] The novel genetic traits are more likely to be passed to the next generation if they increase reproductive fitness. However, in environments that change rapidly, selection of given genotypes in one generation may become maladaptive in the next generation or may be too slow to occur as in species with long generation times. Organisms can respond phenotypically to such changes, and the new phenotype may later become genetically encoded by natural selection (genetic assimilation). These intergenerational effects are not easily explainable with strict principles of genetic inheritance, rather they would invoke the coparticipation of Lamarckian mechanisms in shaping phenotypes. Phenotypic evolution beyond genome evolution can actually occur. Phenotypic plasticity is one source of phenotypic evolution. It refers to the number of phenotypic responses that a single genotype can produce under different environmental conditions. Plasticity allows the organism to rapidly respond and maintain reproductive fitness under variable conditions. Plastic responses may be reversible and of short duration (eg, physiological acclimation) or may be long lasting and somehow imprinted in the molecular memory (eg, some aspects of developmental plasticity). Plasticity may thus aid the initial response to an environmental stressor, with natural selection subsequently refining the phenotype with genetic adaptations to the new environment. If there is low genetic variation underlying the phenotypic response, such response might still have a relevant role in evolutionary change if it were associated with nongenetic inheritance, such as parental (eg, hormones passed by the mother to the offspring) or epigenetic (chemical changes that alter gene expression without any changes in allele frequencies) effects. Biological information is typically considered as being transmitted across generations by the DNA sequence alone, but accumulating evidence indicates that both genetic and nongenetic inheritance, and the interactions between them, have actually important effects on evolutionary outcomes.

Genetic Responses

Genetic recombination occurs during meiosis and produces new allelic combinations that are passed from the parents to the offspring and thus may affect evolutionary processes. A link between environmental stress and recombination has been known for 1 century.[16] Pioneering work on *Drosophila melanogaster* showed that the recombination frequency increased in young exposed to either heat or cold stress, but at near lethal temperature extremes it decreased.[17,18] Similarly, recombination frequency increased with temperature in grasshoppers *Goniaea australasiae* until a point beyond which it decreased.[19] Even acute episodes of either heat or cold stress at critical stages of meiosis increased genetic recombination in *Coprinus lagopus*.[20,21]

Appearance of nonlethal genetic mutations is another potential route through which hormesis may affect evolutionary rate. Ionizing radiation interacts with water to produce reactive oxygen chemicals (eg, free radicals), which can in turn damage biomolecules such as DNA. According to the LNT model, exposure to increased ionizing radiation would result in deleterious effects with no chance for adaptive processes to kick in. Although it is well established that exposure to high doses of ionizing radiation is detrimental for the organism, research on low-dose exposure found different outcomes. By subjecting populations of *Escherichia coli* to selection for high resistance to ionizing radiation,[22] Byrne et al. generated bacteria with a resistance to radiation comparable to that of *Deinococcus radiodurans*, which can absorb doses of radiation over 1000 times the lethal dose for humans without lethality. It has also been found that resistant bacteria had developed genetic mutations that conferred them with higher capacity to repair DNA damage.[22] Experimental repairing of such mutations actually completely removed the radiation resistance.

There are indeed genetic variants that may give rise to hormesis potential. For example, wild-type CB4856 *Caenorhabditis elegans* worms exposed to heat stress survived longer than those worms that were not exposed to heat stress, while this hormetic effect on life span did not emerge in wild-type Bristol N2 worms.[23] Using recombinant inbred lines derived from a cross between wild types CB4856 and N2, it has been found that some of those lines displayed an hormetic effect on life span and the ability to recover from heat shock mapped to a significant quantitative trait locus on chromosome II.[23]

Transposable elements are DNA sequences that can change position within a genome and induce the appearance of deleterious mutations, gene disruption, and chromosome rearrangements. However, activity of transposable elements can also play an important role as promoters of the function and evolution of genomes, such as creation of novel gene variants, chromosome rearrangements, regulation of gene expression, extended telomeric length, population differentiation, and speciation.[24-29] Given that expression and activity of transposable elements may play an essential role in facilitating adaptive organism responses to stressors,[28,30] it might be another potential route through which hormesis generates genetic variation and promotes evolution.

Phenotypic Responses

Hormesis can be seen as a component of phenotypic plasticity and, conversely to physiological acclimation (ie, short-term physiological adjustments to changes in environmental conditions), the phenotypic adjustments induced by hormesis should be long lasting, probably irreversible to a large extent.[6,7]

Exposure to low or mild doses of a given abiotic stressor or contaminant may stimulate transcriptional responses and establish long-term somatic molecular memory that promote survival and even reproduction in some study models.[5,31]

Transmission of chromatin modifications through mitosis (somatic memory) and meiosis (trans-generational memory) is one potential mechanism for long-term storage of prior exposure to low mild doses of a stressor.[31] Growth and development of *Arabidopsis* plants from seedlings exposed to a short mild salt stress treatment were similar to those from seedlings that were not previously exposed to salt stress (controls), yet they had reduced salt uptake and enhanced drought tolerance after a second stress exposure compared to controls.[31] This increased tolerance was associated with small changes introduced in the structure of 4 specific histones and with altered transcriptional responsiveness of several genes.[31] These phenotypic responses are stronger when exposure to the stressor occurs at specific windows of the development period and do not necessarily require that the organism is being exposed again to the stressor at adulthood. For example, exposure of *Drosophila* flies to mild heat stress early in life caused upregulation of heat shock response genes long after the stress was ceased and increased life span when compared to control *Drosophila* flies.[32]

Some molecular responses (eg, transcription rate) can be modulated by transposable elements.[29,33] For example, exposure of *Drosophila* flies (belonging to the isogenic wild type Oregon R line) to a pro-oxidant agent for 5 generations resulted in elevated transcriptional activity of both telomeric and non-telomeric transposable elements and extended their telomeric length.[29]

Hormesis-induced phenotypic responses do not manifest only at the molecular level but can be even substantial for life-history or demographic traits (eg, fecundity and life span). Life-history theory predicts that reproductive hormesis (eg, increased fecundity) will be traded-off against survival perspectives, meaning that increasing fecundity (or life span) would cause a decrease in life span (or fecundity). Thus, the net effect of hormesis on individual reproductive fitness would be negligible. However, many species reproduce once or a few times in life, implying that a small reduction in survival might have minor to negligible consequences for the lifetime reproductive fitness. For long-lived species that have many reproductive events, the relevance of reproductive hormesis might differ from short-lived species. However, a number of studies have found that, within a population, there are individuals that can generate many offspring per reproductive event and live longer than expected compared to individuals that generate less offspring. One reason for this may lie with variation in individual state or phenotypic quality, whereby high-quality individuals may boost both fecundity and longevity because they may better sustain the costs associated. Thus, the point raised about the evolutionary relevance of hormesis does not seem to lie with the occurrence of a trade-off but with when the trade-off would show up.

It has been showed that trade-offs may underlie reproduction hormesis.[34] However, trade-offs did not result in overall decreased reproductive fitness over several generations because continuous exposure of multiple generations to an hormetic dose resulted in higher overall production of offspring. Exposure of *Acheta domesticus* juvenile females to an acute low dose of γ-radiation increased lifetime fecundity, the number of eggs laid over a 4-day period in early adulthood, egg size, and hatching success when compared to females that were not exposed or were exposed to high doses of radiation.[35] Multigenerational exposure during development of *Myzus persicae* aphids to low doses of the insecticide imidacloprid primed offspring to better survive exposure to imidacloprid.[36] This increased resistance to imidacloprid was not due to mutations at target genes associated with insecticide resistance,[36] indicating that such resistance was not probably mediated by genetic responses.

Conclusions

Evolutionary theory sees exposure to moderate environmental stress as one important source of evolutionary change. Thus, it is reasonable to conclude that hormesis might be one engine of evolution because it elicits genetic and phenotypic responses of organisms to moderate stressful events that may promote maintenance of their evolutionary fitness. Some of these adaptive responses appear to be compatible with paradigms such as evolutionary rescue or phenotypic plasticity. Future work should elucidate the environmental conditions under which molecular mechanisms underlying hormesis provide selective advantages.

Acknowledgments

I thank Prof Edwards Calabrese for inviting me to write this short overview about the evolutionary relevance of hormesis and 2 reviewers for providing valuable comments.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iD


David Costantini https://orcid.org/0000-0002-8140-8790

References

1. Bijlsma R, Loeschcke V. *Environmental Stress, Adaptation and Evolution*. Basel, Switzerland: Birkhauser; 1997.
2. Badyaev AV. Stress-induced variation in evolution: from behavioural plasticity to genetic assimilation. *Proc R Soc Lond B*. 2005;272(1566):877-886.
3. Steinberg CEW. *Stress Ecology: Environmental Stress as Ecological Driving Force and Key Player in Evolution*. Dordrecht, Netherlands: Springer Science & Business Media; 2012.

4. Gonzalez A, Ronce O, Ferriere R, Hochberg ME. Evolutionary rescue: an emerging focus at the intersection between ecology and evolution. *Philos Trans R Soc Lond B*. 2013;368(1610): 20120404.
5. Mattson MP, Calabrese EJ. *Hormesis: A Revolution in Biology, Toxicology and Medicine*. New York, NY: Springer; 2010.
6. Costantini D. Does hormesis foster organism resistance to extreme events? *Front Ecol Environ*. 2014a;12(4):209-210.
7. Costantini D.*Oxidative Stress and Hormesis in Evolutionary Ecology and Physiology: a Marriage Between Mechanistic and Evolutionary Approaches*. Berlin, Heidelberg, Germany: Springer-Verlag; 2014b.
8. Agathokleous E, Kitao M, Calabrese EJ. Environmental hormesis and its fundamental biological basis: rewriting the history of toxicology. *Environ Res*. 2018;165:274-278.
9. Costantini D, Borremans B. The linear no-threshold model is less realistic than threshold or hormesis-based models: an evolutionary perspective. *Chem-Biol Interact*. 2019;301:26-33.
10. Forbes VE. Is hormesis an evolutionary expectation? *Funct Ecol*. 2000;14(1):12-24.
11. West-Eberhard MJ. *Developmental Plasticity and Evolution*. Oxford, England: Oxford University Press; 2003.
12. Bonduriansky R, Day T. Nongenetic inheritance and its evolutionary implications. *Annu Rev Ecol Evol System*. 2009;40: 103-125.
13. Pigliucci M, Müller GB. *Evolution: The Extended Synthesis*. Cambridge, MA: MIT Press; 2010.
14. Danchin E, Charmantier A, Champagne FA, Mesoudi A, Pujol B, Blanchet S. Beyond DNA: integrating inclusive inheritance into an extended theory of evolution. *Nat Rev Genet*. 2011;12: 475-486.
15. Jablonka E, Lamb M. *Evolution in Four Dimensions: Genetic, Epigenetic, Behavioural, and Symbolic Variation in the History of Life*. Cambridge, MA: MIT Press; 2014.
16. Hoffmann AA, Parsons PA. *Evolutionary Genetics and Environmental Stress*. Oxford, England: Oxford University Press; 1991.
17. Plough HH. The effect of temperature on crossing over in *Drosophila*. *J Exp Zool*. 1917;24(2):148-209.
18. Parsons PA. Evolutionary rates: effects of stress upon recombination. *Biol J Linn Soc*. 1988;35(1):49-68.
19. Peacock WJ. Chiasmata and crossing-over. In: Peacock WJ, Brock R, eds. *Replication and Recombination of Genetic Material*. Canberra, Australia: Australian Academy of Science; 1968: 242-252.
20. Lu BC.Genetic recombination in Coprinus I. Its precise timing as revealed by temperature treatment experiments. *Can J Genet Cytol*. 1969;11(4):834-847.
21. Lu BC.Genetic recombination in Coprinus. IV. A kinetic study of the temperature effect on recombination frequency. *Genetics*. 1974;78(2):661-677.
22. Byrne RT, Klingele AJ, Cabot EL, et al. Evolution of extreme resistance to ionizing radiation via genetic adaptation of DNA repair. *Elife*. 2014;3:e01322.
23. Rodriguez M, Basten Snoek L, Riksen JAG, Bevers RP, Kammenga JE. Genetic variation for stress-response hormesis in *C. elegans* lifespan. *Exp Geront*. 2012;47(8):581-587.
24. De Boer JG, Yazawa R, Davidson WS, Koop BF. Bursts and horizontal evolution of DNA transposons in the speciation of pseudotetraploid salmonids. *BMC Genom*. 2007;8:422.
25. Oliver KR, Greene WK. Transposable elements: powerful facilitators of evolution. *Bioessays*. 2009;31(7):703-714.
26. Oliver KR, Greene WK. Transposable elements and viruses as factors in adaptation and evolution: an expansion and strengthening of the TE-Thrust hypothesis. *Ecol Evol*. 2012;2(11): 2912-2933.
27. Zeh DW, Zeh JA, Ishida Y. Transposable elements and an epigenetic basis for punctuated equilibria. *Bioessays*. 2009;31(7): 715-726.
28. Chénais B, Caruso A, Hiard S, Casse N. The impact of transposable elements on eukaryotic genomes: from genome size increase to genetic adaptation to stressful environments. *Gene*. 2012;509(1):7-15.
29. Korandová M, Krůček T, Szakosová K, et al. Chronic low-dose pro-oxidant treatment stimulates transcriptional activity of telomeric retroelements and increases telomere length in *Drosophila*. *J Insect Physiol*. 2018;104:1-8.
30. McClintock B. The significance of responses of the genome to challenge. *Science*. 1984;226(4676):792-801.
31. Sani E, Herzyk P, Perrella G, Colot V, Amtmann A. Hyperosmotic priming of *Arabidopsis* seedlings establishes a long-term somatic memory accompanied by specific changes of the epigenome. *Genome Biol*. 2013;14(6):R59.
32. Sarup P, Sørensen P, Loeschcke V. The long-term effects of a life-prolonging heat treatment on the *Drosophila melanogaster* transcriptome suggest that heat shock proteins extend lifespan. *Exp Gerontol*. 2014;50:34-39.
33. Begcy K, Dresselhaus T. Epigenetic responses to abiotic stresses during reproductive development in cereals. *Plant Reprod*. 2018; 31(4):343-355.
34. Ayyanath M-M, Cutler GC, Scott-Dupree CD, Sibley PK. Transgenerational shifts in reproduction hormesis in green peach aphid exposed to low concentrations of imidacloprid. *PLoS One*. 2013; 8(9):e74532.
35. Shephard AM, Aksenov V, Tran J, Nelson CJ, Boreham DR, Rollo CD. Hormetic effects of early juvenile radiation exposure on adult reproduction and offspring performance in the cricket (*Acheta domesticus*). *Dose Response*. 2018;16(3). doi:10.1177/ 1559325818797499.
36. Rix RR, Cutler GC. Does multigenerational exposure to hormetic concentrations of imidacloprid precondition aphids for increased insecticide tolerance? *Pest Manag Sci*. 2018;74(2):314-322.