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# Evolutionary explanations in medicine: How do they differ and how to benefit from them

George A. Lozano *

*Department of Zoology, Institute of Ecology and Earth Sciences, Tartu University, Vanemuise 46, 51014 Tartu, Estonia*

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SUMMARY

Evolutionary explanations, many of which have appeared on the pages of this journal, are becoming more pervasive and influential in medicine, so it is becoming more important to understand how these types of explanations differ from the proximate approach that is more common in medicine, and how the evolutionary approach can contribute to medicine. Understanding of any biological phenomenon can occur at four levels: (1) ontogeny (2) causation, (3) function and (4) evolution. These approaches are not mutually exclusive, and whereas the first two are more common in medical practice, a complete explanation requires all four levels of analysis. Two major differences among these approaches are the apparent degree of immediacy associated with them, and the extent to which they apply to individuals rather than populations. Criticisms of adaptive explanations often arise from a failure to understand the complementary nature of these four types of explanations. Other unwarranted criticisms result from a failure to appreciate that adaptive explanations often apply to populations, not individuals. A third type of criticism is driven by the mistaken belief that adaptive explanations somehow justify morally reprehensible behaviours. Finally, evolutionary explanations sometimes face the criticism of "personal incredulity".

Adaptive explanations must be consistent with basic evolutionary concepts and must adhere to the physical reality of the phenomenon in question. Their value, however, comes not in devising a seemingly rational explanation, but in their predictions. Testable predictions must be explicitly stated and clearly articulated. They must differ from those of arising from other hypotheses and must not only be interesting to evolutionary biologists, but also useful to medical practitioners. Integration of the proximate and the ultimate approaches is possible and potentially beneficial to both evolutionists and physicians, but it requires some basic understanding of our differences and a desire to co-operate.



Evolutionary thinking is becoming more influential and pervasive in psychology and medicine, and several interesting evolutionary papers have recently graced the pages of this journal. For example, Dewar proposed that homosexuality in men is a maladaptive extreme resulting from the "feminization" of male brains that occurred upon the advent of agriculture, when social skills became more important for males [1]. Eagles suggested that seasonal affective disorder (SAD) of women living in high latitudes is an adaptation that decreases the likelihood of conception during the winter, which, in turn, decreases the probability of children being born in the autumn when food supplies are low [2]. Given the positive association between bacterial pathogens and heart disease, and given that iron is an essential element for bacterial pathogens, Summers argued that the overabundance of iron present in modern diets has shifted the balance in favour of pathogens and has led to an increase in the prevalence in heart disease [3]. Finally, yours truly [4] posited that anorexia nervosa was an extreme expression of an otherwise adaptive desire to look youthful in environments in which thinness becomes the best indicator of youth. This is just a small sample, of course, several other adaptive explanations for medical conditions have been proposed in this and in other journals.

The aim of this brief commentary is not to defend any of these hypotheses. Time will tell whether these and other hypotheses are exciting enough to persuade mathematicians to formulate complementary models, theoreticians to articulate alternative or derivative hypotheses, and most importantly, empiricists to test them. Even if these hypotheses are eventually shown to be partially or completely incorrect, they might lead to new work, and in doing so, they might open up new avenues for research. In the spirit of this journal's editorial philosophy [5], judgment must be deferred to the future.

The primary goal of this commentary is to remind our readers what evolutionary or adaptive explanations are, what they are not, and how they differ from traditional medical perspectives. These same ideas have been championed repeatedly and inexhaustibly by Nesse (e.g., [6–9]) and others (e.g., [10], both citation lists could be much longer), but full understanding remains elusive, perhaps because of the narrow nature of our reading habits and

* Tel.: +372 737 5813; fax: +372 737 5830.
*E-mail address:* george.lozano@ut.ee.

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training. Here I add my unique voice to the choir in the hope that it will get the attention of some of the readers of "Medical Hypotheses" who might benefit from a kind reminder. A secondary aim is to pre-empt unwarranted and unnecessary criticisms of evolutionary hypotheses published herein, criticisms that put further pressure on our limited reading time [11], and sometimes obviously result from a misunderstanding of adaptive explanations. Finally, I offer some suggestions for future contributors that might make the presentation of evolutionary hypotheses more palatable and useful to medical practitioners.

## Four levels of analysis

Noble prizes in the sciences are usually awarded retrospectively, once the implications of a given contribution become clearly evident, but in a astounding display of prescience, in 1973 the Nobel Foundation awarded the Nobel Prize in "Physiology or Medicine" to three animal behaviourists and evolutionary ecologists: Karl von Frisch, Konrad Lorenz, and Nikolaas Tinbergen. Only recently have their contributions begun to be incorporated into physiology, and particularly medicine, and much progress still remains. One of Tinbergen's most lasting contributions has been his proposed framework for studying and analyzing behaviour [12], a framework that is applicable to all biological phenomena. Tinbergen pointed out that study and understanding can occur at four levels: (1) Ontogeny: how does it develop within the individual? (2) Causation: what triggers it? Internally and externally, from the molecular or the organismic level, (3) Function: what is its survival value (short-term consequences)? What is its adaptive significance (ultimate consequences)? And (4) Evolution: how did it evolve in the population or the species, related species and ancestral forms? These approaches are complementary, not mutually exclusive, and different people, depending on their backgrounds and interests, will be inclined to answer the same question in different ways. A complete explanation includes all four levels of analysis, and combinations thereof. For example, whereas physiology is included in the second grouping, "causation", environmental physiology or physioecology would also encompass aspects of "function". Physiological comparisons among taxa include the fourth level, "evolution", and changes in physiology during the maturation of an individual would include aspects of "ontogeny".

The first two categories, ontogeny and causation, are often referred to as "how" questions, and the latter two, function and evolution, as "why" questions. However, this division can be misunderstood because semantically, there is nothing preventing us from asking "why" and answering with any of the four types of explanations. For example, let us take a simple question: "WHY do people smoke?" A developmental biologist might answer by focusing on the rearing environment of smokers, potentially since the moment of conception. A neuroscientist or endocrinologist might instead focus on the short-term chemical changes that build the desire and culminate on the act of lighting up. A social psychologist might address peer pressure, and a behavioural ecologist might follow up with a cost/benefit analysis of resisting or giving in to peer pressure. Finally, a population geneticist might examine differences in the effects of nicotine among several populations, depending on their length of their relationship with the tobacco plant, or the presence of particular genes, or study the effects of nicotine on related species. Similarly, questions that might initially be framed using the word "how" can be addressed by any of the four approaches. Therefore, to minimize confusion, it might be better to use another existing categorization, and refer to the first two types of explanations, ontogeny and causation, as the proximate approach and the latter two, function and evolution, as the ultimate approach.

One difference between these approaches is the apparent degree of immediacy associated with them. As their names indicate, proximate explanations attempt to uncover cause-and-effect relationships that are direct and immediate. The immediacy associated with these cause-and-effect relationships ranges from a few seconds to, at the most, an individual's lifetime. The nature of medicine, where immediate relief of suffering usually requires urgent action, tends to favour the proximate approach. In contrast, ultimate explanations are characterized by a deeper understanding, which takes into consideration selective pressures, phylogenetic history, population genetics and other factors that extend beyond the individual and its immediate surroundings to its ancestors, population, history, and ecology. Accordingly, evolutionary explanations can be discarded as being too contemplative and impractical at addressing the urgent task: relieving what ails a patient. Indeed the answers they provide might not be as urgent, but they can be equally or even more important.

Their importance results from the second major difference between ultimate and proximate explanations: evolutionary explanations generally deal with populations, not individuals. Evolutionary explanations are based on population variability, differential survival and/or reproduction, historical selective pressures, risk factors, etc. Hence, they cannot explain why any one individual develops a disease, nor can they lead to individualized treatments. For example, using a global database on incidence of suicides, Saad found support for the prediction, based on sexual selection theory, that the ratio of male-to-female suicides would increase as economic conditions worsen, particularly among "working age" groups [13]. This work says nothing about why any one individual commits suicide, does not explain all types of suicides, nor can it prevent any particular suicide, but it might help governments predict and prevent previously unforeseen and unexpected effects of economic downturns. Evolutionary thinking in medicine could be viewed as overlapping with the field of epidemiology, where long-term planning and solutions are needed but the sense of urgency is not palpable, but it is replaced by a greater degree of importance, given the large numbers of people potentially affected.

## Criticism of evolutionary hypotheses

As in other fields, within evolutionary biology reviewers tend to reject hypotheses that challenge the accepted dogma, and expect new hypotheses to be proposed alongside overwhelming supporting evidence, straddling theory and empiricism. Upon publication, new hypotheses can be the focus of heated debate, mathematical modelling and empirical testing, just like in any other field. As long as these hypotheses do not stray beyond the realm of evolutionary biology, criticisms might not be always civil, but at least they are usually not based on deep misunderstandings. When evolutionary hypotheses deal with humans (behaviour, medicine, psychology), those not trained in evolutionary biology naturally engage in the debate, and several major misunderstandings often arise.

First, criticisms can arise from a failure to understand the complementary nature of ultimate and proximate explanations. To use the smoking example above, a behavioural ecologist might try to explain it using a cost/benefit analysis of resisting peer pressure, only to be "corrected" by a neuroscientist insisting smoking is likely caused by changes in the ratios of various neurotransmitters. However, there is no argument here. Both might be right. Ultimate and proximate explanations are not mutually exclusive; they are just different ways of looking at the same problem. Evolutionary explanations in no way impinge on the predictive powers of molecular, cellular, psychological, physiological, or genetic approaches.

Sometimes this misunderstanding can lead to peculiarly generic criticisms. For example, to counter Saad's evolutionary explanation

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for global patterns of suicides [13], it could be argued that suicide "might then become the synthesis of all possible sins and forbidden desires, with an unsufficiently [sic] identified ego trying to cope between an unleashed greed and a desperate desire to become purely spiritual. This model leaves room for a genetic or epigenetic psychopathological frailty, without excluding the harmful effects of life events (particularly those affecting child's nurturing and first relations) and accepting an important and increasingly understood pathoplastic role of environment and shared culture" [14]. In the preceding sentence, the word "suicide" could easily be replaced by the word "aggression", "infanticide", "addiction" or the originally intended subject, "anorexia", and the criticism would seem just as suitable and as powerful. Indeed, misunderstandings of the very nature of adaptive explanations can lead to criticisms that could easily be used against any hypothesis, evolutionary or otherwise, without offering any alternatives.

Secondly, evolutionary hypotheses are sometimes criticized by drawing attention to the exception. However, these criticisms are akin to questioning the link between smoking and cancer by recalling grandpa, who smoked daily for 70 years and lived to be 91 years old. Furthermore and as already mentioned, adaptive explanations and their predictions address populations, not individuals, so variability is an inherent property of any adaptive explanation. In fact, population variability is the first tenet of Darwin's theory of natural selection. This variation, specifically, heritable variation, is necessary for selection to act upon and for adaptations to evolve. By the way, please note that is the theory of "natural selection", not the theory of "evolution"; evolution is a fact; a fact that is best explained by the theory of natural selection.

Third, particularly when dealing with human behaviour, adaptive explanations face strong opposition from detractors who fail to understand that explanation does not mean justification. For example, adaptive explanations of homicide [15], rape [16], or aggression in general [17], are not well-received by sociologists and psychologists, not because of their logic or predictive powers (or lack thereof), but rather because there seems to be a deeply entrenched belief that evolutionary explanations somehow indicate that these behaviours are "natural" and hence justified. Nothing is further form the truth. Evolutionary explanations do not offer any more moral justification than social, psychological or physiological explanations. They are morally neutral.

Finally, the weakest criticism of evolutionary hypotheses, a criticism that mostly reveals an unwillingness to even trying to understand, is the criticism of disbelief. Dawkins [18] refers to it as "the argument of personal incredulity", and it often begins with "it is hard to imagine/believe..." and similar derivations. For example, referring to Montefiore's [19] argument that adaptation cannot explain the white coats of polar bears because polar bears lack predators, Dawkins [18] explains that this actually means "I personally, off the top of my head sitting in my study, never having visited the Arctic, never having seen a polar bear in the wild, and having been educated in classical literature and theology, have not so far managed to think of a reason why polar bears might benefit from being white". Furthermore, Dawkins points out that even without the benefit of an education in the natural sciences, Montefiore should have been able to come up with at least one adaptive explanation: camouflage is also helpful to a predator.

Nevertheless, not all evolutionary hypotheses are so simple, and indeed, some are hard to imagine. If they were easy, the field would not have to wait for luminaries like Robert Trivers, William Hamilton, Amotz Zahavi, George Williams, or Ronald Fisher, or some of the more modest contributors mentioned in the introduction. Any well-read and articulate evolutionary biologist might be able to come up, apparently off the top of his/her head, seemingly perfectly reasonable adaptive hypotheses for many a phenomenon. Some of these explanations might be well known and generally accepted, others might be largely ignored and highly speculative notes hidden in the literature, and a few might indeed be original and spontaneous.

The latter are immediately tested for common sense, evolutionary speaking, and perhaps quickly dismissed if they fail to agree with various evolutionary concepts. For example, many people still believe that adaptations, particularly behaviours, evolve for the "good of the species", but the idea that selection occurs at the level of the group, as opposed to the individual or the gene, has been discredited since the early 1960s. Hence, any hypothesis that relies on group selection (e.g., [20]) would be summarily dismissed by all mainstream evolutionary biologists. Other such concepts include mal-adaptations, pleiotropic effects and other evolutionary tradeoffs, phylogenetic constraints and history, lag times, units of selection, population genetics, evolutionarily stable systems, etc. Only if a hypothesis makes it past this initial "common sense" screening would it warrant more serious and closer inspection.

One might continue by examining whether the trait in question is variable in the population, which is usually the case whether some of this variability is heritable, if studies on heritability are available, and whether the trait is linked to differential survival and/or reproduction. Should these criteria be met, then there is probably an adaptive explanation for the trait, although it might not be the one being proposed. Adaptive hypotheses simply suggest the mechanisms by which natural or sexual selection act on the existing heritable variance, and try to explain precisely why a trait happens to be adaptive, or maladaptive. Finally, even the most rational evolutionary explanation must pass one final test: adherence with the reality of the phenomenon [21]. Evolutionary hypothesis, reasonable as they might sound, must still obey the laws of physics, and agree with the physiology of the phenomenon in question.

## Testable predictions

Even if an adaptive hypothesis is consistent with basic evolutionary concepts and with the facts about the condition in question, the strength and validity of any hypothesis ultimately depends on its predictive powers. Here is where the presentation of adaptive hypotheses sometimes fails because of two main reasons. First, the power of the evolutionary paradigm can also be a weakness, for it allows the formulation of perfectly reasonable and compelling explanations, and authors sometimes fall to the temptation of presenting them without any explicitly articulated predictions. Hence, potentially useful hypotheses run the risk of remaining nothing more than compelling and interesting stories, which, if ever cited, will be only in the form of "it has been suggested that...", the tacit implication being that they have not been tested, and maybe never will be. It is therefore imperative that evolutionary hypotheses be presented with several clearly stated predictions, explicitly articulating how these predictions differ from those of other adaptive explanations, and suggesting possible tests [22]. The inclusion of clearly stated mutually exclusive predictions makes it more likely that a hypothesis will make the transition from an interesting story into an integral part of active research and development in a given field.

Second, some types of predictions might be adequate for evolutionary biologists, whose aim is to understand adaptation in its many forms, but evolutionary thinkers venturing into the medical realm must also keep in mind medical applications. The inclusion of clinically relevant predictions would make any hypothesis more palatable to those in the medical field. Obviously, this is an area where evolutionary biologists would greatly benefit from co-operation with medical practitioners.

Such co-operation between ultimate and proximate thinkers is possible, but it is also difficult. Evolutionary biologists usually are not particularly interested in how something works, but they

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might be interested on why it happens to work that way, and not another way. On the other hand, proximate thinkers are interested on how something works, and not on why it happens to work that way. The proximate thinker would have to be persuaded that insights from evolutionary biology might help to identify the most likely mechanisms. On the other hand, the ultimate thinker would have to be persuaded that knowledge about mechanisms might result in more clinically relevant evolutionary predictions, transforming what might be a purely academic issue for an evolutionary biologist into a practical tool for medical practitioners. It would seem like a perfect opportunity for partnerships, if only we tried to talk and understand each other, and refrained from unwarranted criticisms that only reveal that we do not.

## Conflicts of interest statement

None declared.

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## References

[1] Dewar CS. An association between male homosexuality and reproductive success. Med Hypotheses 2003;60:225–32.
[2] Eagles JM. Seasonal affective disorder: a vestigial evolutionary advantage? Med Hypotheses 2004;63:767–72.
[3] Summers K. Iron, infection and the evolutionary ecology of heart disease. Med Hypotheses 2001;56:687–90.
[4] Lozano GA. Obesity and sexually selected anorexia nervosa. Med Hypotheses 2008;71:933–40.
[5] Horrobin DF. Ideas in biomedical science: reasons for the foundation of *Medical Hypotheses*. Med Hypotheses 2004;62:3–4.
[6] Williams GC, Nesse RM. The dawn of Darwinian medicine. Q Rev Biol 1991;66:1–22.
[7] Nesse RM, Williams GC. Why we get sick: the new science of Darwinian medicine. New York: Times Books; 1995.
[8] Nesse RM. The importance of evolution for medicine. In: Trevathan WR, Mckenna JJ, Smith EO, editors. Evolutionary medicine. New York: Oxford University Press; 2007. p. 416–32.
[9] Nesse RM, Stearns SC. The great opportunity: evolutionary applications to medicine and public health. Evol Appl 2008;1:28–48.
[10] Charlton BG. A syllabus for evolutionary medicine. J R Soc Med 1997;90:397–9.
[11] Erren TC, Cullen P, Erren M. How to surf today's information tsunami: on the craft of effective reading. Med Hypotheses 2009;73:278–9.
[12] Tinbergen N. On aims and methods in ethology. Z Tierpsychol 1963;20:410–33.
[13] Saad G. Suicide triggers as sex-specific threats in domains of evolutionary import: negative correlation between global male-to-female suicide ratios and average per capita gross national income. Med Hypotheses 2007;68:692–6.
[14] Chiappedi M, Todeschini E. When a mouth is a wound. Med Hypotheses 2009;72:473.
[15] Daly M, Wilson M. Homicide. New York: Aldine de Gruyter; 1988.
[16] Thornhill R, Wilmsen Thornhill N. Human rape: an evolutionary analysis. Ethol Sociobiol 1983;4:137–73.
[17] Archer J. Does sexual selection explain human sex differences in aggression? Behav Brain Sci 2009;32:249–311.
[18] Dawkins R. The blind watchmaker. Essex, England: Longman Scientific and Technical; 1986.
[19] Montefiore H. Probability of god. Trinity Press International; 1985.
[20] Gofrit ON. The evolutionary role of erectile dysfunction. Med Hypotheses 2006;67:1245–9.
[21] Paşca SP, Nesse RM. Vomiting is not an adaption for glaucoma (and Darwinian medicine is difficult). Med Hypotheses 2008;71:472–3.
[22] Platt JR. Strong inference. Science 1964;146:347–53.

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