

How to Test an Evolutionary Hypothesis about Disease

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Adapted from Table 1 in:
Ten Questions for Evolutionary Studies of Disease Vulnerability
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Task 1: Define the object of explanation precisely.

- Q1. **Is the object of explanation a uniform trait in the species, or is the goal to explain variations in a trait among groups or individuals?** Most explanations are about traits all members of a species share. But some are about genetic variations in different subpopulations...things like skin color or vulnerability to malaria. Those require special approaches.
- Q2. **Has the object of explanation been influenced by natural selection?** Or is it something like speaking French or liking Miso soup that is unlikely to have been influenced by selection. Or is it an epiphenomenon such as blood being red? Or a product of genetic drift.
- Q3. What kind of trait is the object of explanation?
- A fixed universal human trait**, such as the narrow birth canal or liking sugar.
 - A facultative trait**, such as the capacity for sweating. Facultative traits are systems shaped by selection that monitor for some situation and express a response that is useful in that situation. They range from blinking, to sweating, to tanning, to changes in the stress response as a result of early exposure to stress (this would be called plasticity because it is longer term).
 - Human genes**, in the most general sense of the term (such as the sickle cell allele or 5HTTR)
 - Pathogen traits**, such as the level of virulence
 - Pathogen genes**, such as those that confer antibiotic resistance
 - Somatic cell lines**, such as those in tumors or the immune system

Task 2: Specify the kind of explanation sought

- Q4. Is **the goal** to explain the evolution of the trait, or its proximate mechanisms?
- Q5. Is the goal to explain the trait's **phylogeny, or the evolutionary forces** that shaped it?

Task 3: List and consider all viable hypotheses

- Q6. **Are all viable hypotheses considered** and given fair consideration, or are some hypotheses neglected, while others receive favored treatment? Scientists sometimes argue like lawyers, advocating for one explanation and disparaging others. This causes problems. It is better to give all possible hypotheses equal treatment, including the hypothesis that the trait under consideration was not shaped by natural selection or that the trait is a product of genetic drift.

- Q7. **Could different vulnerabilities cause the disease in different individuals or subgroups?**
Some diseases always result from the same cause, for instance, cystic fibrosis is always caused by defects in the CFTR genes. But depression can be caused by genes alone, environment alone, or, and more both. Likewise, gastric ulcers can be caused by bacteria, stress, drugs and more. The strong human cognitive tendency to see unicausal explanations must be opposed constantly.
- Q8. What categories of explanation are under consideration?
- Mismatch** of bodies with environments they did not evolve in
 - Co-evolution** with pathogens that evolve faster than hosts can
 - Constraints** on selection, such as time required, genetic drift, and mutation
 - Trade-offs**, especially costs associated with an apparently superior alternative
 - Reproductive success** at the expense of health
 - Defenses** such as fever and pain that cause harm and suffering, but were shaped by selection because they offer protection in certain situations
- Q9. Could **multiple explanations** be correct? Most often there are multiple explanations. And they interact! Fight monocausal thinking!

Task 4: Describe the methods used to test the hypotheses

- Q10. What **methods** are used to test the hypotheses?
- Consistency** with evolutionary theory So, if it is based on group selection, or proposes evolutionary changes in the past few hundred years, it is a nonstarter.
 - Modeling** using quantitative methods Could the trait spread in the population over time?
 - Comparative methods**
 - Comparisons among species This is the gold standard. Is the trait present (or present to a greater degree) in species who live in environments where the trait is useful?
 - Comparisons among subgroups, such as humans from northern and equatorial regions.
 - Comparisons among individuals who vary in a trait such as those with and without the alleles that cause Tay Sachs disease, or tall and shorter individuals
 - Experimental methods**
 - Extirpation or disruption (e.g. gene knock-out studies or blocking fever) Great method!
 - Augmentation (e.g. administration of extra testosterone)
 - Examining regulation of a facultative trait to see if it behaves as predicted If a trait is hypothesized to be useful only in a certain situation, it should be aroused mainly by cues associated with that situation.
 - Observing evolutionary changes in the lab or the field
 - Examining the details of fit** between an observed form and a postulated function 90% of studies rely on this weak method. Too bad, but we have to do what we can.

Ten Common Mistakes in Evolutionary Medicine

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1. Attempting to explain a disease: Instead, reformulate the question as an explanation for a trait that result in vulnerability to a disease.
2. Proposing an explanation based on what is good for the species: This is group selection, an elementary error. Almost all evolutionary explanations must be based on advantages to genes or individuals.
3. Proposing adaptive functions for rare genetic conditions: There are sometimes evolutionary reasons why deleterious mutations stay in the gene pool, but the explanation is hardly ever some useful function of the disease itself.
4. Confusing proximate and evolutionary explanations: This is a common and serious mistake. Knowledge about how the body works can be very useful in assessing an evolutionary hypothesis, but it is no substitute for an evolutionary explanation.
5. Thinking that evidence for learning influencing a trait indicates that no evolutionary explanation is needed: Learning is a capacity shaped by natural selection, and the pathologies that arise from learning mechanisms, such as phobias, are likely to harm fitness.
6. Thinking that evidence for environmental or cultural differences in a trait is evidence against evolutionary influences: Natural selection shaped the behavioral mechanisms that give rise to culture, and environments and culture influence human behavior and fitness strongly. An evolutionary approach to behavior does not imply that behavior is somehow “determined by the genes,” only that the mechanisms that give rise to behavior and culture were shaped by natural selection. These mechanisms obviously are capable of profound flexibility, with attendant benefits and costs.
7. Confusing genetic explanations, especially behavioral genetic explanations, with evolutionary explanations: Traits need evolutionary explanations whether or not individual variations arise from genetic variations.
8. Failing to consider all of the alternative hypotheses: This is very common and very serious. All too often an author will argue for one possibility without making the alternatives explicit
9. Assuming that evidence for one hypothesis is evidence against another: Multiple factors may all contribute to a complete explanation and they may interact in complex ways. Correct explanations often incorporate multiple explanatory factors.
10. Presenting all the evidence in favor of a pet hypothesis and all of the evidence against other hypotheses, instead of offering a balanced consideration of all evidence for and against all hypotheses: This is rhetoric, not science. It is observed commonly, for good reasons arising from human nature, not just in testing evolutionary hypotheses but across the range of sciences. Nonetheless, such advocacy should be avoided.