Afterword

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Healthy body, unhealthy mind?

"The manipulation of host phenotype by parasites is a ubiquitous phenomenon…not limited to a few unusual species of purely academic interest" (Poulin and Levry 2012). Imagine Poulin, Levry, and others in this volume are right about that. That would mean that for at least 500 million years, parasites have been trying to make hosts do things they would not otherwise do. Such pressure must have left an indelible mark on host evolution. Here we speculate that this "ghost of manipulation past" is likely to have had a profound effect on the way hosts control their own behavior, with consequences for health and wealth as important as those listed by Poulin and Levry.

There are two ways hosts can protect themselves from behavior attack. One way is to kill or incapacitate the causal pathogen. The other way is to counter the manipulation itself, either by making behavior control systems less vulnerable to attack, or by recalibrating things to accommodate the manipulation. Immunologists study the first kind of defense; next to nothing is known about the other kind, but we contend anti-manipulation defenses must exist. We will be surprised if they do not become central to behavioral biology and neuroscience in the years to come.

The easiest way to see this is by analogy. The hygiene hypothesis in immunology comes in various forms but broadly speaking it posits that lack of exposure to infectious agents increases susceptibility to allergies, asthma, and other autoimmune problems. A growing body of literature supports the view that the developing immune system needs stimuli from infectious agents, symbiotic bacteria, and parasites in order to perform adequately. For example, in a large double-blind placebo study, infants of Ugandan mothers treated with anthelmintics were twice as likely to develop infantile eczema (Mpairwe et al.). Why do immune systems "need" pathogens to function properly? Immune systems are constantly being manipulated by pathogens. Helminths, for example, secrete substances that dampen mammalian immune responses. The evolutionary version of the hygiene hypothesis posits that immune systems evolved to cope with this down regulation. Remove that down regulation and you have excessively aggressive immune reactions. Increasingly it really looks like there is something in this. Give people with autoimmune disease worms and they get better (Broadhurst et al.).

Imagine that behavioral control systems are similarly adjusted by natural selection for the presence of manipulating parasites. The neural pathways and endocrine systems that underlie sensory and decision-making processes are prime targets for pathogens seeking to modify the behavior of their hosts to enhance transmission. How much of our neural complexity is a necessary defense against manipulative invaders? How much of the enormous redundancy is to provide system level functionality if part of the system is attacked? How much of the complex process of wiring a brain during development is to prevent pathogen re-wiring? Hormone and neurotransmitter concentrations can be key behavior modifiers; are base levels set to accommodate parasite-derived manipulation?

And what is the consequence of sudden removal of parasites and pathogens from hosts evolutionarily prepared for encounters with manipulative parasites? How many behaviors in a hygienic world are maladaptive, in the same sense that allergies are maladaptive immune responses? Behaviors associated with disease transmission, such as promiscuity, aggregation, activity levels, boldness, and predator avoidance, are likely to be the target of parasite manipulation. Is it possible that without parasites, behavior control systems perform in ways they were not designed for?

Consider for example the apparently profound impact of *Toxoplasma* infection on humans, ably summarized by Poulin and Levri. *Toxoplasma* infection is staggeringly common today, even in rich countries; in the conditions under which humans evolved, infection with *Toxoplasma* and many other animal-maintained parasites must have been at least as frequent. Humans should be well defended against *Toxoplasma*-induced behavioral alterations. We are a dead-end host for the parasite, so we should have won the evolutionary arms race with *Toxoplasma*: the other side was not partaking.

What are we to make of the variety of behavioral phenotypes induced in contemporary humans by *Toxoplasma* infection? At first glance, some look like pathology (men more likely to be jealous) but some look suspiciously useful (men more likely to be vigilant), and indeed it is relatively easy to imagine that in historical times, many *Toxoplasma*-induced traits conferred fitness advantages on human hosts (even jealousy). Did natural selection recalibrate human behavior control systems so that they were optimal in the face of manipulating parasites?

If so, we see intriguing dilemmas for applied biology. Again by analogy with the hygiene hypothesis, when might modern medicine and farm practice aimed at removing pathogens or preventing infections be maladaptive for a host that is evolutionarily prepared to encounter specific parasites and the suite of altered mechanisms that ensue? When do we need our parasites?

We are not arguing that patients should not be treated against infectious disease (!) or that we should abandon modern hygiene (!!). But if our logic is correct, it could be that solutions to what we nowadays view as behavioral pathologies lie in identifying the mechanisms by which parasites manipulate host behavior. Could administration of analogs of those mechanisms offer solutions to problems in mental health?

We are also not arguing that farm animals should be left unprotected from disease—pathogen burdens can be greatly elevated in intensive farming situations, with clear effects on yield. But are there conditions where farm animal welfare would be improved if it were possible to mimic the manipulative pressures that might come from more "natural" disease burdens or from parasite species present until recently? For instance, stereotypies, the repeated expression of sometimes maladaptive behavior brought about by the inability to perform more normal behavior, is a common feature of zoo animals. Is this because zoo animals have been deprived of the regulatory effects of behavioral manipulation by natural pathogens?

A different issue concerns animals reared in captivity for release as part of reintroduction programs for conservation. Normally, we strive to release animals with a full bill of health. The scrupulously clean living conditions and hygienic, plentiful supplies of food are free from the array of pathogens wild-living conspecifics will naturally be exposed to. Is such hygiene misplaced? We could be disadvantaging the long-term health of the animals if they fail in the pre-release phase to develop immunity to pathogens they will encounter in the wild. Could animals raised without stimulation from manipulative parasites have a poorly developed behavioral repertoire? They may be missing out on key behavioral adaptations that promote dispersal and recolonization. Parasites such as *Toxoplasma* have the capacity to alter temperament traits such as boldness and tendency to explore. Without this manipulation some individuals may fail to disperse and recolonize—behaviors that might deliver advantages in a conservation context.

We are only too well aware of the speculative nature of our arguments (but if you can't speculate in a commentary in a David Hughes book, when can you speculate?). If we are ball-park correct,

then parasite manipulation of host behavior could become a key element in the nascent fields of evolutionary medicine and applied evolution. As always, it is a mistake to equate the natural or evolved state as that which maximizes societal good. But understanding selective forces helps generate hypotheses, structure thinking and unify otherwise disparate biological observations. Behavioral variation in our farm and companion animals, and indeed in us, is hugely important for human happiness and health. If much of this variation is due to defenses against parasites past, and the mechanisms involved can be understood, novel approaches to mental health, animal welfare and conservation should be possible.

Credit. These speculations were stimulated by Zuk (2007, chapter 4).

References

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