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# Editorial overview: Insect behavior and parasites: From manipulation to self-medication

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Kelli Hoover is a professor in the Department of Entomology, Center for Chemical Ecology, and Center for Pollinator Research at Penn State University. Her research addresses insect-microbial symbioses; interactions between baculoviruses, insects, and their host plants; forest tree pollinators; and ecology of the invasive spotted lanternfly.

Melting caterpillars rain disease upon munching herbivores on plant leaves below. Wasps burst from the heads of their hosts to escape the crypt that holds them. Caterpillars fight off predator attacks in defense of the organisms who will eventually kill them. Nature has created horrors just as jaw-dropping as those conjured by the most creative science fiction authors. Although these phenomena are not universal among parasites, adaptive manipulation has evolved many times in all major lineages of parasites [1]. In this issue, we review altered behavior of insect victims by parasites, from adaptive host manipulation that benefits the parasite, to self-medication that benefits the host.

Evidence that a phenotypic change in host behavior is manipulated by the parasite rather than an adaptive response of the host requires evidence that the behavior enhances fitness of, and is genetically controlled by, the parasite (the extended phenotype (Dawkins 1982)). Also, to confirm that phenotypic changes in host behavior fit the 'adaptive host manipulation hypothesis' proffered by Holmes and Bethel [2], there must be evidence of enhanced transmission rates as a result of this manipulation [1].

This special issue includes eight reviews of the current literature. The topics covered include: host manipulation by parasites (and parasitoids), entomopathogens (fungi and viruses), and plant viruses; the potential mechanisms of manipulation; self-medication in social and solitary insects; and ecological considerations about energy flow in food webs altered by parasite manipulators. Note that although these phenomena have been observed for many years, ~~however~~ the underlying physiological mechanisms, as well as the net fitness effects, remain to be discovered for most described cases of manipulation.

Kelly Weinersmith focuses on studies that examine the span of parasite manipulation in arthropods. She discusses attempts to address questions about the evolution of mechanisms of these manipulations. Her review highlights the fascinating examples of spiders parasitized by *Polysphincta* wasps and ants infected with *Ophiocordyceps* fungi; the latter topic is covered in greater detail in this issue by one of the investigators of this system, Charissa de Bekker. de Bekker summarizes the recent advances of the molecular mechanisms behind the manipulation as well as the histological changes that underlie the alterations in behavior. In this system infected ants climb up their host plant and bite down on the vein of a leaf to keep from being displaced at death, allowing time for the fungus to sporulate from the ants' bodies, raining infectious spores onto the trails used by conspecifics. While no conclusive mechanistic answers are yet known for this manipulation, integrative research efforts using behavioral ecology, phylogeny, genomics, transcriptomics, metabolomics, and fossil records have increased our knowledge of this system considerably.

Shelly Adamo discusses how parasites and pathogens use different approaches to manipulate their hosts, including co-opting existing behavioral control systems, or by using the host's neural networks to produce the desired behavour. She explains that by altering hormone levels, parasites can gain access to neural circuits allowing them to induce complex behaviors. She presents details about two groups of parasitic manipulators that appear to exploit host behavioral control systems: the baculoviruses (insect-specific viruses) and parasitic wasps that turn their hosts into bodyguards.

Two reviews in this issue discuss different aspects of self-medication in social and solitary insects, which are behaviors in response to parasites that enhance the fitness of the host rather than the parasite. Jacob de Roode and Mark Hunter present criteria for distinguishing altered behaviors of infected insects that represent a defense rather than parasite manipulation. Several insect groups can use a broad range of nutritional or toxic phytochemicals to medicate themselves or their kin, and this behavior can be used for therapy for those already infected or as a prophylaxis to prevent infection under high risk conditions. Marla Spivak and coauthors provide examples of self-medication among social bees (bumblebees, stingless bees, and honey bees) in which the consumption or use of plant compounds play a documented role in parasite defense and colony health. Both reviews stress that while advances have been made, there are critical areas that require more in-depth investigation. Information is lacking on when self-medication is considered prophylactic versus therapeutic, identification of costs to the host and to the colony in social insects, and development of theoretical models that can predict the role of infection risk in selecting for the evolution of medication behaviors.

Manipulation by parasites even includes plant viruses that can alter the behavior of insect vectors and/or their plant host. Kerry Mauck and coauthors evaluate the experimental evidence for plant virus components implicated in driving insect vector behavioral manipulation by direct (vector) and indirect (plant) effects. This review follows an elegant study by Mauck *et al.* [3] showing that cucumber mosaic virus (CMV) has effects on the quality and attractiveness of one of its host plants for two different aphid vectors of this widespread plant pathogen. The virus increases attractiveness of infected plants to aphids by increasing the release of volatile emissions from infected plants, while also reducing host-plant quality. In this review, the authors connect findings and methods from pathology of plant viruses with studies using functional genomics to investigate virus manipulation. They also discuss new approaches that could lead to improved understanding of mechanisms of host and vector manipulation by plant viruses.

Takuya Sato and coauthors explore broader ecological questions about how host manipulation by parasites alter predator–prey interactions in ways that can change energy flow in trophic cascades. They argue that by manipulating hosts, parasites indirectly mediate the intensity of predator–prey interactions, which can alter energy flow across food webs; they refer to this energy flow as manipulation-mediated energy flow (MMEF) and discuss the ecological implications of these manipulations.

It has been known for over 100 years that baculoviruses induce their hosts to die in elevated positions on the tree or plant on which they are feeding, which is referred to as 'tree top disease'. Because baculoviruses cause their hosts to liquefy at death, melting cadavers rain virus particles onto the foliage below, enhancing horizontal transmission to new hosts [4]. But this is not the only host behavior manipulated by baculovirus infection. In this issue, Vera Ros discusses tree top disease and hypermobility (enhanced locomotion), both of which boost virus transmission. She provides the details of molecular evidence for viral genes (*egt* and *ptp)* that can control these behaviors, and how light (positive phototaxis) or negative geotaxis may be involved. Interestingly, enhanced locomotion and tree top disease appear to be controlled by different viral genes that originated in ancestral hosts. Moreover, different viral genes appear to induce tree top disease in different host-virus systems, suggesting that manipulation of host behavior by baculoviruses may have evolved multiple times or may be the result of co-opting the natural behavior of the host in response to hormonal signals.

Genetic control of mechanisms of host manipulation by parasites has not been determined in most systems, in large part due to the difficulties of directly testing the role of parasite genes in altering host behavior. Fortunately, molecular techniques are available to generate gene knockouts in many baculoviruses. Although one or more genes in baculoviruses appear to trigger tree top disease (death at elevated positions) in lepidopteran hosts (Ros 2019), manipulation may include the pathogen taking advantage of the hosts' natural behaviors and its endocrine system (Adamo 2019 this issue; Hoover *et al.* 2011). Because viruses are dependent on their host's metabolism, they should benefit by co-opting host compounds or using existing signaling molecules to enhance their own fitness, rather than requiring synthesis of new compounds by the host, which can be costly. This may explain the selection pressure for baculoviruses to acquire and maintain *egt* and *ptp* genes from their ancestral hosts [5,6].

Parasites exploiting the host's endocrine system is a clever way to manipulate its host and may be common. Weinersmith reports (this issue and references therein) that spiders parasitized by *Polysphincta* wasps are induced to spin the web that is used by the wasp larvae to make its cocoon for pupation, and this behavior appears to be induced by an increase in 20E titer in the spider. As is the case with the baculovirus that infects the gypsy moth, *Polysphincta* parasitoids exploit a developmental hormone produced by the host.

As discussed in this issue, altered host behavior in response to parasites has been reported for numerous insects and other species; while many advances in understanding these complex interactions have been made, the mechanisms controlling these behaviors and how they evolved remain elusive.

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