

SMXLs), will enable us to gain a better insight into molecular mechanisms underlying the roles of strigolactones and karrikins, as well as their role in plant adaptation to abiotic stresses. These efforts in turn will provide us a promising avenue for developing improved stress-tolerant crop plants.

#### Acknowledgments

We apologize to those colleagues who have contributed to this field but were not cited because of space limitations.

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## Manipulators live better, but are they always parasites?

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**A recent study reports partner manipulation for an interaction that was considered a reward-for-defence mutualism. Secretions of lycaenid caterpillars altered ant locomotion and aggressiveness, likely by manipulating dopaminergic signalling. This study opens the question whether such manipulation is common and whether manipulation necessarily characterises an interaction as parasitism.**

In a new ground breaking study Hojo *et al.* [1] report partner manipulation for an interaction that previously was considered to be a reward-for-defence mutualism. Lycaenid caterpillars secrete a metabolically valuable liquid from their dorsal nectary organ (DNO) and are tended by ants, which feed on this reward and defend the caterpillar against predators. Recently, Hojo *et al.* discovered that the DNO secretion decreases ant locomotion activity and increases the aggressiveness of the ants. Manipulated ants also were more likely to return to tend the caterpillar [1]. In simple terms, the caterpillar gains a reliable standing army of defending ants, whereas the ants pay the cost, because they become dependent. The authors conclude that ‘reward-for-defence interactions that have tradition-

ally been considered to be mutualisms may in fact be parasitic in nature’ [1].

This phenomenon shows astonishing similarity to a partner manipulation effect that my group discovered in another reward-for-defence mutualism: *Acacia* myrmecophytes (obligate ant–plants) manipulate the digestive capacities of their obligate ant inhabitants (*Pseudomyrmex ferrugineus*) to make them dependent on host-derived food rewards. Chitinase in extrafloral nectar (EFN), which these plants secrete to nourish their ant defenders, was found to block invertase (sucrose-hydrolyzing) activity in

#### Glossary

**Arginine vasopressin:** a mammalian peptide hormone that circulates in the blood stream and that, if taken up into the brain, has been associated with social behaviour and sexual motivation.

**Dopamine:** a biogenic amine functioning as neurotransmitter in the brain and as local chemical signal outside the brain that is associated with reward learning in virtually all animal species investigated so far.

**Epigenetic effect:** an epigenetic effect alters the probability and/or intensity of gene expression, usually via changes in the degree of methylation of promoter regions or in histone structures.

**Mutualism:** an interaction among organisms of different species that enhances the fitness of all partners.

**Myrmecophyte:** a plant that lives in a mutualistic relationship with ants and is continuously inhabited by a specific ant colony.

**Parasitism:** a symbiotic interaction among organisms of different species that increases the fitness of one partner (the parasite) at the cost of the other partner (the host).

**Partner manipulation:** a phenotypic or behavioural change in one organism that is under the genetic control of another organism.

**Symbiosis:** the prolonged living together of organisms of different species.

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1360-1385/

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the gut of workers, thereby rendering the ants dependent on sucrose-free *Acacia* EFN [2]. Another example is a pollination mutualism: Wright *et al.* reported that caffeine in floral nectar of *Citrus* and *Coffea* species enhances the capacity of honeybees (*Apis mellifera*) to memorise the respective rewards [3]. The common scheme that arises from these observations is that food rewards alter the behaviour of a partner organism, at the obvious benefit of the manipulator. Nevertheless, the different authors draw different conclusions concerning the nature of the manipulated interaction. Hojo *et al.* consider the resulting interaction to be ‘parasitic in nature’, whereas Wright and colleagues [3] and my group [2] consider the interaction to be (still) mutualistic.

Taken together, these studies pose at least two interesting questions: (i) how common are manipulation effects in the various categories of interspecific interactions and (ii) does manipulation necessarily turn the resulting interaction into parasitism? Indeed, manipulation effects are commonly reported for trophically transmitted parasites. Interestingly, one of the few cases of adaptive host manipulation by a parasite for which the molecular mechanism has been deciphered shows a striking similarity to the observations made by Hojo *et al.* The protozoan, *Toxoplasma gondii*, uses at least three molecular pathways to manipulate the behaviour of its mammalian hosts. (i) *T. gondii* hypomethylates the arginine vasopressin promoters in the medial amygdala of rats: an epigenetic manipulation that could cause a stronger activation of vasopressinergic neurons after exposure to cat odour and, thus, initiate the reversion of fear into attraction that characterises the manipulation by *Toxoplasma* [4]. (ii) *T. gondii* enhances the plasma levels of the steroid hormone, testosterone, in infected male rodent or human hosts; and, (iii) it enhances the levels of the neurotransmitter, dopamine, in the brains of infected rodents [5,6]. The genome of *Toxoplasma* contains two genes for tyrosine hydroxylase, which catalyzes the rate-limiting step in the synthesis of dopamine [7]. In consequence, dopaminergic neural cells in *Toxoplasma* cysts release elevated amounts of dopamine into the brain of an infected host [8]. In combination with the epigenetic manipulation, the enhanced levels of dopamine and testosterone can explain the increased aggressiveness and fearlessness that is frequently observed in infected male rodents and humans [5]. Strikingly, Hojo *et al.* also reported an enhanced aggressiveness of manipulated ants. This behavioural change was associated with altered dopamine levels in the brains of the ants, albeit ants that had access to DNO secretions contained lower, rather than higher levels of dopamine [1]. The different directions in the changes in dopamine levels in manipulated mammals and ants clearly represent an interesting research subject *per se*. However, most interestingly, partner manipulation via an interference with dopamine levels in the neuronal system of a partner organism has now been reported for two phylogenetically distant organisms: an insect and a protozoan.

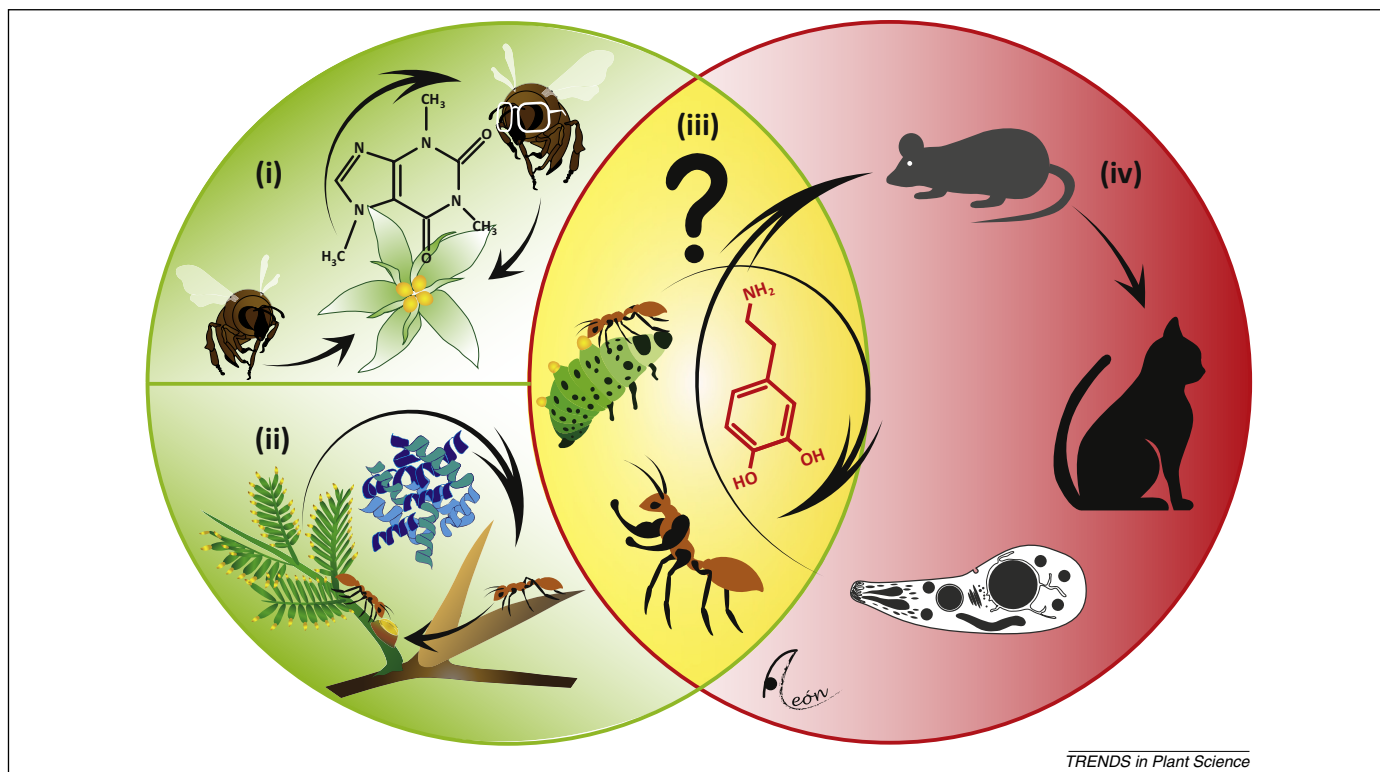
Are there any other examples of manipulation, and do they promote mutualistic or parasitic interactions? Baculoviruses cause ‘Wipfelkrankheit’ or ‘tree-top disease’, a seemingly ‘Zombie’-like behaviour of caterpillars.

Healthy caterpillars at a certain developmental stage hide in the soil and pupate, whereas virus-infected individuals climb to the highest parts of their host tree where they die, liquefy, and release the virions. Using transformed viral strains, Hoover *et al.* [9] demonstrated that the viral gene *ecdysteroid-uridine diphosphate – glucosyltransferase* encodes an enzyme that inactivates the caterpillar’s molting hormone by transferring a sugar moiety to it, thereby suppressing molting behaviour. More recently, van Houte *et al.* found that the climbing behaviour of baculovirus-infected caterpillars is associated with a positive phototactic response [10]. Unfortunately, different viral strains and different host species were used in these two studies. Therefore, it remains an open question whether the observed mechanisms represent alternative or complementary strategies of baculoviruses to manipulate their host caterpillar.

Toxoplasmosis increases the predation risk for the infected rodents and tree-top disease ultimately kills the infected caterpillars, outcomes which clearly characterise these interactions as parasitism. However, signs of manipulation have also been reported for interactions that are considered to be mutualisms. Besides the above-mentioned plant–ant and plant–pollinator mutualisms [2,3], a further example is provided by N-fixing rhizobia. Rhizobia cannot leave the nodules in the roots of certain plant species once they have differentiated into bacteroids [11]. Most interestingly, the plant genetically controls this differentiation step [12], which therefore represents a manipulation of the bacterium by the plant. However, bacteroids are more efficient than undifferentiated bacteria at fixing nitrogen [11], an effect that is likely to benefit both, the host plant and the ‘trapped’ bacteroids. Similar to manipulated plant–ants, the manipulation at the proximate level obviously benefits the manipulator. Nevertheless, manipulation might sufficiently improve reward production as well as the efficiency of their overall exchange, thus both organisms would gain a fitness benefit. In this scenario, the interaction would be a mutualism.

Returning to the most recent example by Hojo *et al.*, an interesting next step would be to perform a cost–benefit analysis for the ant. How does the nutritional benefit that the ant colony obtains from the DNO secretion balance against the ‘lost opportunities’ in terms of reduced foraging activity? If the net nutritive balance remains positive for the ants, the interaction might be considered to be a mutualism. It also would be interesting to investigate whether the ants are really ‘trapped’ by the caterpillar and how they could escape, in case the net outcome of the manipulation is negative for the ants. In the end, each individual caterpillar has to attract new ants and, thus, the evolution of avoidance behaviour by the ants seems feasible.

In summary, Hojo *et al.* discovered that a lycaenid caterpillar alters dopamine levels in the brains of ants that are feeding on a nutritive reward. Because the behavioural change in the ant is under the control of the caterpillar, this interaction represents a new example of partner manipulation. The described phenomenon shares molecular elements with the manipulation of dopamine levels in the mammalian brain by the parasite, *T. gondii*, and is



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**Figure 1.** Partner manipulation - shared elements with different outcomes. Manipulation effects discussed in this spotlight article are (i) the enhancement of the memory of bees by caffeine in floral nectar [2], (ii) the inhibition of invertase activity in ant guts by invertase in extrafloral nectar [3] and the manipulation of the behaviour of ants by lycaenid DNO secretions (iii) or of rats by *T. gondii* (iv); the latter two cases being mediated by interference with dopaminergic signalling in the brains of ants [1] or rats [7,9]. Manipulation enhances partner fidelity in the cases (i–iii) and the likelihood of successful transmission of *T. gondii* to its final, feline host in the case (iv). Authors of the different studies have suggested that manipulation maintains either mutualism (green background: i, ii) or parasitism (reddish background: iii, iv). The question mark and yellow background indicate that more work is needed to confirm whether the interaction is mutualistic or parasitic in nature.

functionally equivalent to the manipulation of ants or pollinators by plant-derived rewards (Figure 1). It remains to be studied to which degree similarities at the molecular level result from convergent evolution. Most importantly, partner manipulation might be more common than assumed, particularly among those interactions that traditionally are considered to be mutualisms. Fitness effects for manipulators and manipulated partners will have to be studied if we aim to understand when manipulation makes mutualism work better or converts it into parasitism.

#### Acknowledgements

I thank Sandhya Sekar and Susan Milius for the discussions that motivated me to write this Spotlight and CONACyT de México (grant no. 251102) for financial support.

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