Bipolar drug turns foraging ants into scouts

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Whether foraging for food, caring for young, or defending the nest, the worker castes of carpenter ants toil selflessly for their queen and colony. Now, biologists have figured out how to make some of those worker ants labor even harder, or change their very jobs in ant society, all by making small chemical modifications to their DNA.

The finding calls attention to a new source of behavioral flexibility, and drives home the idea that so-called epigenetic modifications can connect genes to the environment, linking nature to nurture. The work is "a pioneering study establishing a causal link between epigenetics and complex social behavior," says Ehab Abouheif, an evolutionary developmental biologist at McGill University, Montreal, in Canada. "These mechanisms may extend far beyond ants to other organisms with social behavior."

Insect biologists have long debated whether the division of labor in these sophisticated species with castes is driven by colony needs or is innate. Evidence in honey bees had pointed toward a genetic difference between queens and workers. In the past several years, however, work in both honey bees and ants had indicated that epigenetic modifications—changes to DNA other than to its sequence of bases (or DNA "letters")—influence caste choices, indicating environmental factors can be pivotal. But subsequent research about one type of change, methylation, led to contradictory conclusions.

Daniel Simola, a computational biologist at the University of Pennsylvania, knew almost nothing about ants when he joined Shelley Berger's epigenetics lab in Philadelphia, Pennsylvania. But he did want to explore how epigenetics contributes to an organism's ability to respond to environmental changes, and decided to use one of the ants, *Camponotus floridanus*, that Berger worked with for such studies. Like other carpenter ants, this species has two worker castes: smaller minors, and bigger majors with larger heads (see photo).

One essential job for workers is foraging, and Simola and his colleagues quantified how much the two castes did by marking individual ants, letting them go hungry for a day, and recording how often they searched for and retrieved food.

Minors foraged a lot more than majors and were fast at the job, particularly when they were young, Simola found. It's not clear what majors do, though some have suggested that given their size, they may defend the nest or carry large food items.

He and his colleagues then tested whether epigenetic differences were responsible for this division of labor.

An earlier study by Berger's group indicated that variations in the number of a chemical entity called an acetyl group on proteins called histones, which serve as the scaffolding for DNA, might be important. Acetylation seems to loosen a histone's tie on DNA, allowing genes nearby to be more active.

So Simola and his colleagues treated different sets of minors and majors with chemicals that affected the addition or removal of acetyl groups from histones. One, a mood-stabilizing drug for bipolar disorders, inhibits the enzyme histone deacetylase, which removes acetyl groups, damping gene activity. Another inhibits an enzyme that adds acetyl groups. When a treatment resulted in greater histone acetylation in the ants, minors revved up foraging and even started taking on the job of the scout caste, looking in new places for food. Young majors also began to forage regularly and scout, something they typically don't do, the team reports today online in *Science*. "We can reprogram the behavior," Simola concludes.

"It was surprising that they were able to manipulate the foraging behavior through molecular mechanisms so cleanly," Abouheif says. Changes in older ants of either caste were more subtle, suggesting a window of malleability exists in younger workers.

Moreover, the work shows the power of histone acetylation, in addition to methylation. "DNA methylation has become nearly synonymous with epigenetics," says Brendan Hunt, an insect geneticist at the University of Georgia in Griffin. "This research brings needed attention to the importance of other epigenetics marks, like histone modifications."

"We finally have a mechanism to understand 'nurture' in molecular terms," says Gene Robinson, a geneticist at the University of Illinois, Urbana-Champaign, who studies caste determination in honey bees. The ant study, he adds, highlights "how the environment gets under the skin to affect gene expression, and consequently, neural activity and behavior."

*(Video credit: AAAS/*Science*)*

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