Podcast Interview: David Hughes

PNAS: Welcome to Science Sessions. I'm your host Chris Samoray.

Microbes are abundant throughout the natural world, and some parasitic microbes can manipulate the behavior of their hosts. David Hughes, a professor of entomology and biology at Pennsylvania State University, studies such parasite-host relationships. Hughes focuses on a parasitic relationship in which a fungus infects and controls the behavior of carpenter ants in order to reproduce. Hughes and colleagues examined the mechanisms that enable the parasitic fungus to control ant behavior. They found that fungal cells that spread throughout the ant body appear to coordinate to manipulate host behavior. The work, which was published in PNAS, garnered the 2017 Cozzarelli Prize in Biomedical Sciences. Hughes describes how the parasitic fungus uses the ants for reproduction.

Hughes: As the ants are walking through the forest, the fungus is attaching to their bodies and then over a period of 12-18 hours, literally blowing a hole through the ant's body as they enter in through the cuticle. Once inside the ant's body, they replicate over a period of 2-3 weeks, at which point the ant is back inside the colony and getting on with its daily activities. And then at the end of this replication cycle the fungus controls the ant to leave the colony. It's impossible for the fungus to transmit inside the nest because of the hygienic behavior the ants have. In order for it to transmit, it needs the ant to get out. It uses the ant as a vehicle. What we found is that the manipulation is so precise, that these individual ants die above the foraging trail of the colony, and then the spores are produced from the dead body and then they rain down on the individual ants. So, the manipulated ants are essentially shooting spores down on their sisters.

PNAS: Before the fungal spores can spread to other ants, however, an infected ant must bite and hold onto a substrate, like a leaf or twig. From there, the fungus will release its spores. It is a critical point in the lifecycle of the fungus, Hughes says. Using microscopy, 3D reconstructions of the host and parasite tissues, and machine learning techniques, the researchers studied this point in the lifecycle of the fungus, and found that parasitic fungal cells, which envelop and penetrate the ant muscles, form complex networks that direct the ants' movement. Hughes explains.

Hughes: A pivotal point in this relationship is having your ant bite onto the substrate. And so, we see these fungi abundantly inside the mandibular muscles. The head of an ant is about 65% muscle. But we also found them in other parts of the muscles throughout the body. They target the muscles by causing a separation between tightly packed muscles. So, the muscles are now further apart from one another, and this is probably important because once they're separated the fungal cells can form a 3D network. And so, since this is a manipulator, you can imagine it like a puppet master pulling strings.

PNAS: Another key observation, Hughes says, is that the fungus infects only the muscles of the ant; the brain is spared.

Hughes: It seems as if this fungus has just gone straight to the muscles. So, this was important also in the paper we were discovering that the fungi did not enter into the brain. And so, this individual organism seems to be pulling on the strings peripherally, without having to go inside the brain. And it probably does so by producing chemicals that cause contractions. So, the model that we think is happening here is the fungal cells get in, proliferate in the body, encircle the ant's muscle, and then start to produce a range of chemicals that cause this contractive behavior. And it's this contractive behavior the affects their ability to move, and eventually propels them outside the nest to the eventual resting place, which is the underside of those leaves.

PNAS: Hughes says it's remarkable that an organism without a brain controls an organism with a brain, and refers to the fungus as a neural engineer. The findings challenge conventional theories that parasite manipulation of host behavior requires invasion of the host brain. Still, Hughes thinks that the brain must be involved in some way. The next step, he says, to is to identify the point at which the ant is no longer an ant, or as Hughes puts it, "a fungus in ant's clothing."

Hughes: So, at which point do you stop being an ant? At which point do you become the tool of the fungus? And I'd like to know if there's a distinct transition between that. How do you control the behavior, and it must involve the brain in some way, when you're not in the brain? How do those chemicals go across the blood-brain barrier? How does such a thing evolve? A lot of our work is in a phylogenetic context. We know that these ant-manipulating parasites evolved from beetle ancestors—so, parasites in beetles and then before that they were in plants. So, what are the genetic toolkits involved to control behavior? And then we also know that many ants are not manipulated. They're not infected. So, what is it that prevents this fungus from taking over and controlling it?

PNAS: I asked Hughes how he felt about receiving the Cozzarelli prize.

Hughes: It's a great honor. It's absolutely wonderful. It's very nice to have a recognition like this for myself and for the coauthors. It's a very interdisciplinary paper. It combines natural history, machine learning, and serial imaging. And it's really nice that the academy and PNAS has recognized this.

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