

# Fatal Attraction

Some protozoa infect the brain of their host, shaping its behavior in ways most suited to the pathogen, even if it leads to the suicide of the host

BY CHRISTOF KOCH



**THE ANCIENT DEBATE** surrounding the existence of free will appears unresolvable, a metaphysical question that generates much heat yet little light. Common sense and volumes of psychological and neuroscientific research reveal, however, that we are less free than we think we are. Our genes, our upbringing and our environment influence our behaviors in ways that often escape conscious control. Understanding this influence, the advertisement industry spent approximately half a trillion dollars worldwide in 2010 to shape the buying decisions of consumers. And extreme dictatorships, such as that in North Korea, remain in power through the effective use of insidious and all-pervasive forms of propaganda. Yet nothing approaches the perfidy of the one-celled organism *Toxoplasma gondii*, one of the most widespread of all parasitic protozoa. It takes over the brain of its host and makes it do things, even actions that will cause it to die, in the service of this nasty hitchhiker. It sounds like a cheesy Hollywood horror flick, except that it is for real.

We know that illness in general can slow us down, incapacitate us and, in the worst case, kill us. Yet this organism is much more specific. Natural selection has given rise to pathogens that infiltrate the nervous system and change that system's wiring to achieve its ultimate pur-

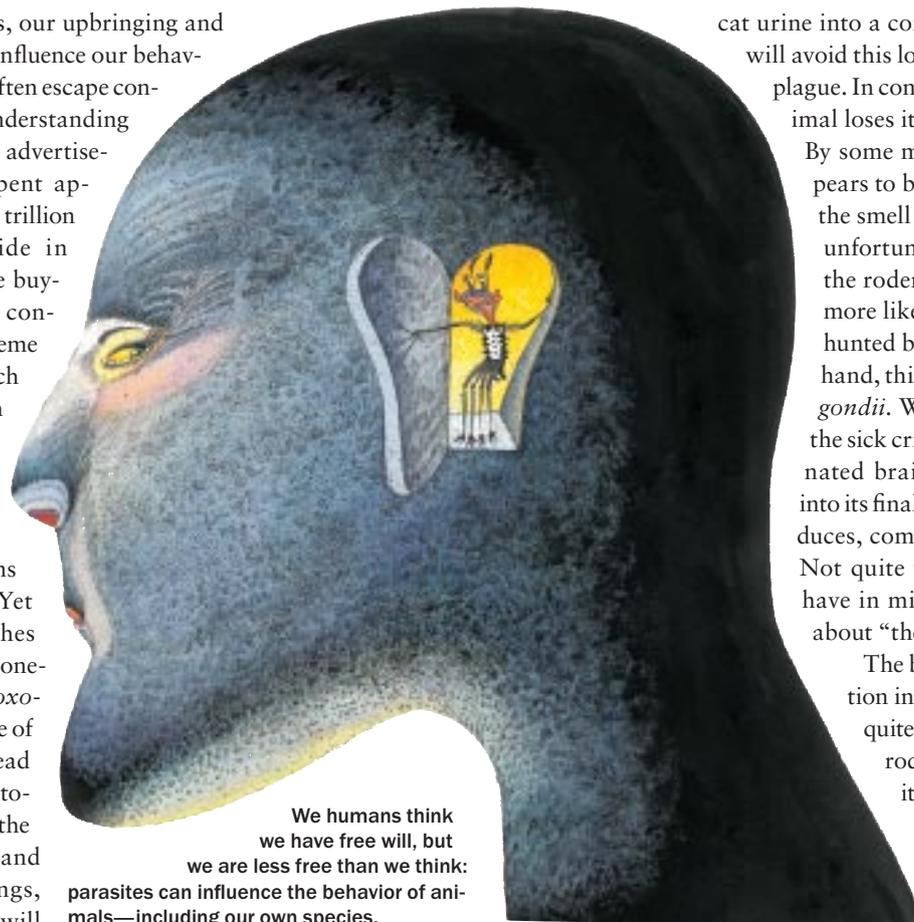
pose, replication—like a computer virus that reprograms an infected machine.

Such is the case with *T. gondii*. It sexually reproduces only in the intestines of cats yet can maintain itself indefinitely in any warm-blooded animal. Infected cats

ity, these invaders make the host's brain do things counterproductive to its own survival.

Toxoplasmosis has been most thoroughly studied in rats and mice. Both species have a deep-seated, innate fear of cats for obvious reasons. Spray a bit of cat urine into a corner, and the rodent will avoid this location, well, like the plague. In contrast, an infected animal loses its innate fear of cats. By some measures, it even appears to be mildly attracted to the smell of felines. This is an unfortunate turn of events for the rodent, because it is now more likely to be successfully hunted by a cat. On the other hand, this is a great deal for *T. gondii*. When the cat devours the sick critter and its contaminated brain, *T. gondii* moves into its final host, where it reproduces, completing its life cycle. Not quite what the romantics have in mind when they write about "the circle of life"!

The behavioral manipulation induced by *T. gondii* is quite specific. The infected rodent doesn't look sick; its weight is normal; it moves about normally, possibly a bit more frantically than other mice; it grooms itself; and it interacts routinely with its conspecifics. Think how different this case is from what happens in rabies, another nasty infection. The animal loses its instinctual shyness, aggressively attacking others (the proverbial mad dog), thereby spreading the rabies virus through its bite. But because *T. gondii* can reproduce only in felines, it wants its host to be eaten by cats, not by just any carnivore. And be-



We humans think we have free will, but we are less free than we think: parasites can influence the behavior of animals—including our own species.

shed millions of their oocysts in their feces. Taken up by all kinds of animals, including dogs, rodents and humans, they infect muscle and the brain to escape attacks by the host's immune system. Hidden away, they remain dormant as cysts, surrounding themselves with a tough cell wall. Yet this quiet stage of infection, called toxoplasmosis, is deceptive. Violating all rules of good hospital-

CHRISTOF KOCH (Koch): JACK UNRUH (head and earwig)

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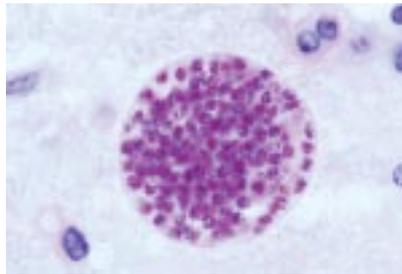
cause cats hunt live prey and do not eat carrion, *T. gondii* must not immediately kill its temporary host.

### Rodents Aren't Superheroes

How does *T. gondii* effect its insidious changes in the host? Experiments by Joanne P. Webster of Imperial College London, Robert Sapolsky of Stanford University and others have shown that infected rats or mice do not turn into the murine equivalent of Siegfried, the hero of Wagner's *Ring* who knew no fear. No, they still avoid open spaces, remain nocturnal creatures, retain their aversion to the urine of other predators and learn to fear a tone associated with a foot shock. Might the protozoa have stunted their smell? After all, if they cannot smell anything anymore, they would not know how to avoid places smelling of cat urine. But infected mice still avoid food if it smells different—an aversion that arose partly because for centuries humans have been trying to control rodents by poison. The infected mice also respond appropriately to the smell of their littermates.

Clues about how the parasites affect the animal come from several observations. First, the density of cysts in the amygdala is almost double that in other brain structures involved in odor perception. Parts of the amygdala have been linked to anxiety and the sensation of fear. Second, the genome of *T. gondii* contains two genes related to mammalian genes involved in the regulation of dopamine, the molecule associated with reward and pleasure signals in the brain, including in ours. So perhaps the creepy protozoa makes suicidal activities, such as hanging around places frequented by cats, feel more pleasurable for the infected rodent?

What elevates this vignette about evolution and life in the wild to epic proportions for humanity is that about a tenth of the U.S. population is infected by *T. gondii* (in some countries, such as France, the in-



**A cyst of *Toxoplasma gondii* resides in the brain. Can these silent invaders, which remain for life in the brain of the infected individual, control us without our awareness?**

fection rate is seven to eight times higher, possibly because of the widespread consumption of uncooked and undercooked meat). Human toxoplasmosis is usually considered to be symptom-free (what doctors refer to as asymptomatic). Exceptions are patients with a weakened immune system and the unborn (hence the need for pregnant women to avoid cleaning cat-litter boxes).

Science has known for a long time that schizophrenic patients are two to three times more likely to carry antibodies to *T. gondii* than are controls who are not schizophrenic. Furthermore, antipsychotic drugs that block the action of dopamine, such as haloperidol, commonly used in the treatment of schizophrenia, are also effective in combating toxoplasmosis in both rats and people. And some infected adults go on to develop psychotic symptoms similar to schizophrenia. Little is known about the mode or site of action of this pathogen in the human brain. The exact link between *T. gondii* and psychiatric dis-

eases is tantalizing but remains murky.

Recent claims go so far as to argue for a role of *T. gondii* in shaping distinct cultural habits, depending on the rate of infection in the population. A prospective study tracking the road safety in Czech recruits during their 18 months of compulsory military draft found a rate of accidents six times higher in affected drivers. Are the young men with toxoplasmosis infection simply slowed down? Or do they drive more aggressively?

In my November 2009 column, I described the discovery by cognitive neuroscientists that the feeling of freely willing an action (called authorship or agency) is a subjective, conscious sensation no different, in principle, from the conscious awareness of seeing the azure blue sky or feeling the sharp pain of a toothache. When I engage in a dangerous pursuit, such as taking the end of the rope on a steep section of a granite wall in Yosemite Valley while climbing, I feel as if “I freely decided” to do so, whatever this might mean in a metaphysical sense. Yet my action is most likely caused by an inexhaustible multiplicity of factors not accessible to my conscious introspection, including, yes, possibly some tiny single-celled parasites lodging in my brain and making me act out their silent commands. The wonder of it all. **M**

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### (Further Reading)

- ◆ **Bugs in the Brain.** Robert Sapolsky in *Scientific American*, Vol. 288, No. 3, pages 94–97; March 2003.
- ◆ **The Effect of *Toxoplasma gondii* on Animal Behavior: Playing Cat and Mouse.** Joanne P. Webster in *Schizophrenia Bulletin*, Vol. 33, No. 3, pages 752–756; 2007.
- ◆ **Manipulation of Host Behavior by *Toxoplasma gondii*: What Is the Minimum a Proposed Proximate Mechanism Should Explain?** Ajai Vyas and Robert Sapolsky in *Folia Parasitologica*, Vol. 57, No. 2, pages 88–94; 2010.