

WHAT THE CAT DRAGGED IN: A Closer Look at *Toxoplasma gondii*

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Jaroslav Flegr teaches evolutionary biology at Charles University in Prague, where I visited him in September. In recent years, the parasitologist's work has attracted increasing attention as the subject of numerous popular journal articles, new studies at places like Stanford and Imperial College London, and zombie apocalypse conspiracy theories. The more I learned about Flegr's research, the more convinced I became that my body was playing host to a colony of sinister parasites. The more I needed to talk to him.

Toxoplasma gondii, the parasite Flegr studies, is a protozoa that lives in cats, rats, birds, and other warm-blooded creatures. In most of these organisms, the parasite reproduces asexually by a process called endodyogeny, in which two daughter cells form inside, and then consume, a mother cell. But in cats—both domestic and wild—*T. gondii* can reproduce sexually. When infected cats defecate, they excrete microscopic cysts containing *T. gondii* zygotes. This means that if, like me, you've changed a litter-box or played in a neighborhood sandpit, you too could be carrying around a legion of cat-loving protists.

What's the big deal? After all, we've known for a long time that the vast majority of the cells in our bodies don't belong, strictly, to us. Estimates from the National Institute of Health hold that our bodies' nonhuman genes could outnumber our own by a factor of 100-to-one. We have around five hundred species of microorganisms in our guts alone; some help us digest carbohydrates, prevent allergies, defend against disease, and stimulate cell growth, while others, such as *Helicobacter pylori*, can cause negative symptoms like ulcers and gastritis. Even our mitochondria—the parts of cells responsible for respiration and energy production—probably began as free-living bacteria that our cells incorporated through endosymbiosis¹ maintaining their own distinct genome.

The difference between these symbionts and *T. gondii* is that the latter can cause a disease called toxoplasmosis. For almost a century, pregnant women and people with compromised immune systems have been warned against the disease, which can result in severe birth defects and flu-like symptoms. In critically immunodeficient people, such as sufferers of HIV and AIDS, toxoplasmosis can be lethal. But in healthy, non-pregnant people, a toxoplasmosis infection is brief and relatively asymptomatic. The *T. gondii* parasites that live on in the body after such an infection were thought to be latent freeloaders like many other of our microfloral friends. They were considered pretty harmless—at least until Jaroslav Flegr began publishing staggering new studies about the effects of *T. gondii* on the human brain.

Since he started researching the parasite in the 1990s, Flegr's studies have turned up some

¹ A mutually beneficial relationship between two organisms, one of which lives inside the other.

ominous results. They suggest that the parasite can significantly increase the probability of schizophrenia, traffic accidents, and suicide in infected people, and could be indirectly responsible for millions of deaths per year. One study shows that *T. gondii* hosts who have a negative Rh factor (or, a minus sign in their blood-type) are over six times likelier to have traffic accidents than uninfected or Rh-positive patients.² Another showed that shrinkage of the cerebral cortex, a common hallmark of schizophrenia, increases at an exponential rate in parasite hosts.

As if this isn't frightening enough, Flegr also posits that *T. gondii* has the capacity to subtly change our personalities—how we act, what we look like, who we find attractive. What's even weirder is that the parasite produces almost diametrically different reactions in women and men. When I asked him about it, Flegr said, "We found that *Toxoplasma*-infected women are more warm-hearted, more open, and more friendly, [while] infected males are frankly less open. They prefer to be alone." Just as infected women become more extroverted, trusting, and rule-abiding, infected men grow more shy, suspicious, and disobedient. "There are also differences, for example, in dressing habits," he went on. "Infected women prefer very expensive and new dresses while the opposite is true for men—just look at me!"



CATTERBRAINED

In fact, Flegr became interested in *T. gondii* the same way I did: by suspecting that he had it. Flashback to the 1980s in then-Czechoslovakia, where young Jaroslav walks the streets of Prague amid protesting students, communist officers, and Soviet tanks. During Normalization, he also spends a brief research stint in Kurdistan, where the Iran-Iraq war and the Anfal genocide campaign imperil even the lives of civilians. Yet somehow, in two of the most dangerous places for a vocal and indiscreet dissident, amid widespread violence and wider-spread surveillance, Flegr wasn't scared. He wasn't even fazed. One day in Kurdistan, a bullet whizzed by him in the street. "For me, it was nothing," he told me. "It was normal."

It was during this period that the scientist picked up *The Extended Phenotype* by evolutionary biologist Richard Dawkins. The book is a kind of Genesis for parasitologists, purporting that an organism's phenotype should include not only the ways that genes manifest inside the body, but also the ways they manifest outside the body, in relationship to the environment. In other words: "An animal's behaviour tends to maximize the survival of the genes 'for' that behaviour, whether or not those genes happen to be in the body of the particular animal performing it."

Already working in parasitology and familiar with *T. gondii*, Flegr put two and two together. "When I thought about [the extended phenotype], I realized that *Toxoplasma* was a good candidate for manipulation activity," he said. "I started to think about my behavior and my psychology, to think that some patterns and traits can be influenced by *Toxoplasma*."

² The effects of *T. gondii* in Flegr's studies are decidedly more pronounced in Rh-negative subjects; the somatic environment of such subjects allows for faster growth of the parasite. Such research, thinks Flegr, may help illuminate the physiological function of the RhD molecule and the origin of RhD polymorphism.

What makes this parasite “a good candidate for manipulation activity?” For starters, the fact that, in the body of a rat, *T. gondii* can switch the neurochemical response for fear with the response for sexual pleasure. Joanne Webster at Imperial College London found that infected rats become not only less averse to cat urine, but actively attracted to it. Once in the rodent’s body, the parasite plants cysts in its brain, liver, and muscle tissue. In the presence of a cat, the infected rat receives a jolt of dopamine, convincing the animal that its predator is actually an object of desire—and thereby increasing the probability that the parasitic cyst will end up in the body of a hungry house-pet, where it can undergo sexual reproduction. *T. gondii* literally has the power of mind-control. Webster’s abstracts often look like pitches for a new Cronenberg movie.

But this data wasn’t around when Flegr started his research. He was going on a hunch that his strange behavior was the result of the *Toxoplasma* in his brain. In the mid-1990s, years after he first encountered Dawkins, his suspicions were confirmed. According to his findings, most *T. gondii*-infected, cat-owning men like himself exhibited a markedly decreased fear-response. He conducted psychological studies on his students at Charles University; since an estimated one in three people has a latent form of toxoplasmosis, the student body provided plenty of test subjects. “Plus,” Flegr added, grinning, “laboratory mice are very expensive.”



TOXOPLASMA GONZO

I was acutely aware, walking into the Biological Sciences building at Charles University, past cabinets of taxidermied weasels and up a flight of empty marble stairs, that this was the alma mater of Franz Kafka. I was here to interview a scientist about a cat-loving microbe that may or may not be hijacking my mind. Talk about surreal.

I’d learned about the parasite a few months prior, when a recently-published comprehensive review of Flegr’s findings received a lot of media attention. I’d heard an NPR feature, read an article in the *Atlantic*, and scrolled through hundreds of blog posts, tweets, and Facebook statuses about the parasite. Everyone I knew seemed to think she had it—from cat-owners and gardeners to people who just exhibited some of the characteristics of their *T. gondii* sex stereotypes. According to Flegr, “[*T. gondii*] concerns everybody because...everybody can suppose that he or she is infected.”

When he started his research over twenty years ago, the world was far less ready to listen. His theories sounded fringy and incredible and *scary*. No one wants to hear that her life is in the hands—er, flagella—of a microscopic parasite. But scientists today are more accustomed to the idea that our bodies are not exclusively our own, that we exist as a kind of aggregate of passengers and symbionts, that the human genome is just one piece of the puzzle of our lives. The Human Microbiome Project, an initiative of the National Institute of Health launched in 2008, seeks to identify and understand our microbial flora and their effects on human health and disease. In June, the NIH announced that a calculated 10,000 microbial species share our bodies, and that between 81% and 99% of the genera have now been identified.

Douglass Morse, an evolutionary biologist at Brown, says of Flegr's theories, “

The story about rewiring rats' brains to become attracted to cats fits a not uncommon situation (for the most part known in invertebrate) where parasites manipulate host behavior in a variety of ways that optimize their passage to an alternate host.” While many of Flegr's ideas remain to be adequately tested on humans (a significantly taller order than testing on laboratory mice), there are myriad examples of parasites affecting the nervous systems of animals. Flegr's more radical predictions “are not beyond the realm of possibility,” says Morse. “That is, I think they're credible, and for the most part, likely.”

But there's a big difference between finding a proposition credible and accepting it wholesale and then running with it. Articles in plenty of publications—including the *NY Times Magazine* and *Esquire*—have equated toxoplasmosis with the condition of the “Crazy Cat Lady:” the archetypal spinster who keeps dozens of cats, avoids human contact, and always smells a little like pee. You know the stereotype: *The Simpsons*' Eleanor Abernathy, Sylvia Plath's Ella Mason, the woman Alex murders in *A Clockwork Orange*. As an almost pathological cat-lover, I was worried that *T. gondii*—if I had it—would have me hoarding kitties by middle age. But while the parasite attracts infected rodents to cats, Flegr's writings don't mention feliphilia as a symptom in humans.

When I asked him about the Crazy Cat Lady complex, Flegr replied, “I think that it has nothing to do with *Toxoplasma*.” In fact, it may have less than nothing to do with *Toxoplasma*; while infected men find the odor of cat urine more appealing than uninfected men, according to Flegr's research, infected women find the smell unusually offensive. Infected women may actually, in some cases, be *less attracted to cats*.

An attractive explanation for this phenomenon, says Flegr, is that women develop an aversion to cats in order to protect potential offspring from a *T. gondii* infection. Women harboring the latent parasite do not typically pass the parasite on to their children (while female mice often do), but an infection during pregnancy can cause severe and even deadly birth defects. It makes sense that the body of an infected woman would try to stave off the dangers of congenital toxoplasmosis in her offspring.

But, compelling though this narrative may be, Flegr thinks there's more to the story. Infected women's increased aversion to cats, he claims, is just one of a slew of reactions that fall under the heading of “stress responses.” By this hypothesis, the psychological changes that accompany latent *Toxoplasma* are not direct responses to the parasite. Instead, these psychological changes stem from the mild chronic stress that latent *T. gondii* wreaks on the body. The parasite does not exactly rewire our brains, as it does in rats or mice; instead, it exposes our bodies to long-term subliminal stress just by infringing on our tissues.

The stress hypothesis would also explain the sex-specific behavioral responses to *T. gondii*. Here's an excerpt from an article by Flegr published last November by the Public Library of Science:

In contrast to men, who seem to use more individualistic and antisocial (e.g. aggressive, hostile) forms of coping with stress, women are more likely to seek and provide social

support, join with others, verbalize towards others or the self. A recent biological (evolutionary) theory similarly distinguishes between the male “fight-or-flight” response and the female “tend-and-befriend” reaction to stress following from the strong need of women to protect children and maintain social relationships.³

This concept—of behavioral polarity in men and women—makes me very uneasy. Talking about it with Flegr, I felt like I had traded the mythology of the Crazy Cat Lady for the mythology of gender essentialism, with its approval-seeking women and its crabby, selfish men. The explanation didn’t jell with my ideas of gender neutrality or political correctness, of the separability of gender—a person’s culturally and socially informed sexual identity—from sex—a person’s reproductive anatomy.

Additionally, the “tend-and-befriend” model itself may be oversimplified, a possibility that most *T. gondii* scientists don’t address. Shelley Taylor posited tend-and-befriend in 2000, asserting for the first time that women and men respond to stress in clearly and qualitatively different ways. But it’s hard to know to what extent gendered responses to stress are biological, and to what extent they’re produced by culturally gendered stressors. Taylor’s critics have accused her of “[missing] an opportunity to address the role that discrimination, oppression, and power imbalances play in women’s behaviors”⁴ and of eliding the frequent and manifold conditions wherein women respond to stress by demonstrating fight-or-flight behaviors and men by forming affiliative coalitions with other men and women. Since current understandings of *T. gondii* rely heavily on the tend-and-befriend theory, it’s easy to feel dubious of scientists’ emphasis on gender contrasts.

But Flegr isn’t claiming that latent toxoplasmosis turns women into party girls and men into crotchety old hermits. Psychological changes are generally very subtle, personal, and slow to manifest, occurring over many years. It’s probable that the physiological differences in men and women do affect their responses to *T. gondii*—but sex is just one of countless factors that determine how a person reacts to being parasitized.



KITTY CORNERING

Over the course of our interview in Flegr’s cozy, unkempt office, I became less and less worried about *Toxoplasma gondii*. The risks are real, especially for an Rh-negative young person like me. It’s even possible that the parasite has been inside me all my life, that I’d been infected through my babyhood cat, Spot. But Flegr, a parasite host and the leading specialist in the field, seemed largely unbothered by the prospect of psychological manipulation. The idea that we share our bodies with thousands of other species doesn’t scare so much as excite him.

³ Flegr J, Lenochová P, Hodný Z, Vondrová M (2011) Fatal Attraction Phenomenon in Humans – Cat Odour Attractiveness Increased for *Toxoplasma*-Infected Men While Decreased for Infected Women. PLoS Negl Trop Dis 5(11): e1389. doi:10.1371/journal.pntd.0001389

⁴ Pitman, G E (2003) Evolution but no revolution: The tend and befriend theory of stress and coping. In Reviews. *Psychology of Women Quarterly*, 27, 186-196.

“Evolutionary psychology is my favorite subject,” he told me. “Fifteen years ago when we started, I was surprised by how much we know about mice and rats. But there are so many interesting and important things that concern our species that we do not know. A lot has been done since then, but everything is still relatively new.”

But as one of the first parasites whose effects on human psychology have been studied and publicized, *T. gondii* is at the center of a lot of sensationalism and alarm. The parasite’s possible correlations with suicide, reckless driving, and schizophrenia are scary—and we should take them very seriously. But no one should drop their pets off at the pound anytime soon. In fact, most cases of the alleged “feline menace” don’t involve direct contact with cats at all, but with infected water, garden soil, unclean vegetables, and undercooked meat. Flegr himself has two outdoor cats as well as two young children. He just keeps his home clean and eats his meat well-done.

Does toxoplasmosis still make me nervous? Sure. But until we know more, our collective hypochondria is as much a source of “mild, chronic stress” as anything. I don’t know if I have *T. gondii*, but I plan to find out later this month, when I return to Charles University to participate in one of Flegr’s studies. I don’t know if it matters if I have it, or if my diagnosis will change the way I think about myself and my body. I hope not.

Because the fact is that we don’t know why we act the way we act. The interplay between our genes and our environment is constant, elaborate, and largely unknown. At every moment, we are responding to stimuli we don’t even know about in ways we don’t yet understand. Flegr’s work advances the cause of learning about our world, ourselves, and the tenants that share our body’s ecosystem.