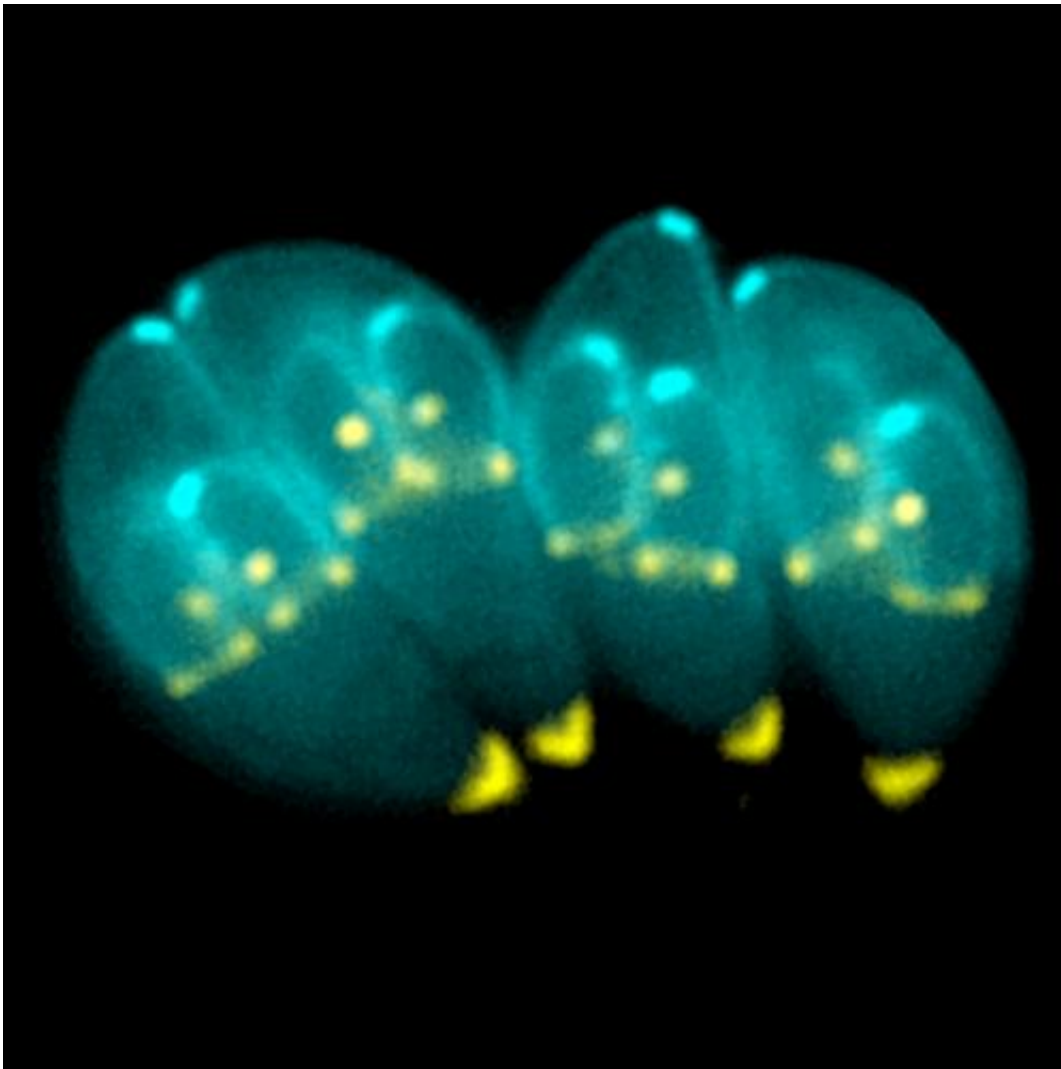


New study identifies drug that can reverse hyperactivity induced by parasitic infection

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Toxoplasma gondii. Credit: Wikipedia

When rodents get infected by *Toxoplasma gondii*, the single-celled brain parasite that causes toxoplasmosis, they become hyperactive risk-takers. In findings published this week in *mBio*, researchers show for the first time that it's possible to reverse that behavioral change. Surprisingly, the study also showed that the restoration of normal behavior resulted from reducing inflammation—and not from reducing the amount of parasites in the brain.

Toxoplasma can infect any mammal. People become infected after exposure to the feces of an infected cat, through a blood transfusion, or by eating undercooked and contaminated meat. Most [healthy people](#) show no symptoms, though the parasite can cause body aches and fever, similar the flu.

The parasite can be extremely dangerous when passed from mother to fetus during pregnancy. Infection can cause miscarriage or stillbirth, and infected infants have a risk of seizures, jaundice, eye infections, and enlarged liver. Some infected children may have symptoms like hearing loss or mental disability that don't appear until puberty.

The new *mBio* paper builds on previous discoveries from the laboratories of microbiologist Bill Sullivan, Ph.D., and biochemist Ronald Wek, Ph.D., at the Indiana University School of Medicine and senior authors of the new study. Their research had previously shown that guanabenz, an old drug for high blood pressure, can significantly reduce the number of *Toxoplasma* [brain](#) cysts in chronically infected mice.

"Guanabenz allowed us to ask an intriguing question people have been wondering about for years," says Sullivan. "If brain cyst counts are lowered, then would the changes in behavior caused by *Toxoplasma* also be reduced?"

The Centers for Disease Control and Prevention estimates that about 40

million people in the United States are chronically infected with *Toxoplasma*. The parasite usually lives quietly in cysts throughout the body, but when the immune system is suppressed, the microbe begins replicating. Reactivation of infection causes rapid tissue damage and neurological symptoms that can become life-threatening. In humans, chronic *Toxoplasma* infection has also been linked to increased risk for schizophrenia.

Jennifer Martynowicz, an MD/Ph.D. student in Sullivan's laboratory, used guanabenz to treat two strains of mice with chronic *Toxoplasma* infections. Consistent with previous work, the drug reduced the number of brain cysts in BALB/c mice. However, brain cysts were not reduced in C57 mice, a strain known to be more susceptible to the infection.

Remarkably, the new study showed that *Toxoplasma*-induced hyperactivity was reversed in both strains of mice. Surprised by that observation, Martynowicz examined the infected mouse brains and found that the drug had also reduced inflammation in both strains of mice.

Microbiologists have suggested multiple ways in which the parasite can manipulate host behavior, such as by changing neurotransmitter levels or directly manipulating host cells with secreted parasite proteins. But the *mBio* study suggests future research should also investigate the role of the host's [immune system](#) in those behavioral changes, too.

"Our study showed that regardless of the level of parasite burden, we can still reverse the behavior changes," says Martynowicz. "We need to be more concerned about what the host is doing during longstanding [infection](#), as our results indicate that it's the immune response driving some of these changes." The next challenge, she says, is to better understand that connection.

More information: Jennifer Martynowicz et al, Guanabenz Reverses a Key Behavioral Change Caused by Latent Toxoplasmosis in Mice by Reducing Neuroinflammation, *mBio* (2019). [DOI: 10.1128/mBio.00381-19](https://doi.org/10.1128/mBio.00381-19)

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