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# Infection with Toxoplasma gondii may lead to Alzheimer's



Parasitic infections can be a nightmare, especially when they interfere with your breathing, eyesight, or digestive tract. But some parasites cause no symptoms in most people with a working immune system. Toxoplasma gondii (or Toxo for short) is one of them, and according to the Cente for Disease Control (CDC) sixty million people in the United States may be infected with it. This parasite eventually ends up in the brain, but no one knows how it affects the brain cells or the brain connections of healthy humans. Dr. Margaret Bynoe, professor of immunology in the Department of Microbiology and Immunology, led a study published in the Journal of Neuroinflammation to determine the effect of chronic Toxo infection on the brains of healthy mice.

Epidemiological studies have linked infectious diseases to neurological disorders. For instance, Toxo causes toxoplasmosis, which in some cases can lead to behavioral symptoms popularly referred to as the "crazy cat lady syndrome". A meta-analysis study found that people who had Toxc antibodies in their blood, a sign of a past infection, were at a greater risk of developing schizophrenia. Other epidemiological studies point to a possible link between Toxo infection and Alzheimer's. However, the evidence on the latter has been contradictory as some studies have found a link while others have not.

To begin to solve this controversy, Bynoe's group infected wild-type laboratory mice with Toxo, and then looked for signs of Alzheimer's disease in their brains. One of the hallmark characteristics of Alzheimer's is the appearance of aggregates made up of beta-amyloid, small protein fragments derived from a much larger protein involved in normal brain function. These aggregates form naturally, and they are usually eliminated before they have time to accumulate. In Alzheimer's disease, this process becomes a lot less efficient, which allows for the aggregates to build up and affect how neurons function and how they communicate with each other. Bynoe's group found beta-amyloid aggregates in the brains of mice after as little as 15 days post-infection, and the number of aggregates increased as infection progressed.

Another hallmark of Alzheimer's disease is the alteration of a protein known as Tau. Neurons have an internal support structure that helps transport nutrients from one part of the neuron to another. Tau stabilizes this structure. In Alzheimer's, the tau protein becomes increasingly phosphorylated, preventing Tau from stabilizing the support structure of neurons. Bynoe's group found that Tau phosphorylation increased after infection with Toxo. They also observed more neuronal death in the infected mice, along with several behavioral abnormalities, including memory loss, lack of interest in social interactions, and a reduced sense of smell. The neuronal receptor N-methyl-D-aspartate (NMDAR), whose job is to strengthen communication between neurons and mediate learning and memory, also decreased significantly over the course of the infection.

**Different models, different results**

Bynoe's study contradicts others that show that Toxo infection ameliorates signs of Alzheimer's in mice due to the activation of phagocytic cells that "engulf" the amyloid aggregates. "Symptoms might improve temporarily, but eventually the infection might become detrimental. Infected neurons will try to find a way to overcome the infection by creating additional sites where they can still carry out nerve conduction. Eventually, they will become overworked and will die," says Bynoe.

**A non-linear path**

A Toxo infection is not a surefire way to end up with Alzheimer's disease. For example, Toxo was found in the serum of seventy percent of France's population in the 1970s, but in 2012 the prevalence of Alzheimer's was only three percent among French people sixty years or older.


Bynoe believes that while Toxo may not be the underlying cause of Alzheimer's in the general population, it may initiate pathological events that over a lifetime can result in Alzheimer's -like symptoms.

A separate study found that whether disease occurs after infection with Toxo depends on the presenc of genes that increase susceptibility to disease, as well as environmental factors such as other infections, the microbiome, and stress.

"After our study was published I started to get a lot of questions from people who were fearful," says Bynoe. "We don't want to cause panic, but I think people should be aware. I mainly wanted to attract attention to how Toxo might alter the brain, and to the fact that it may not be a harmless infection under all circumstances."

Toxo may be implicated in Parkinson's disease, schizophrenia, obsessive-compulsive disorder, and Tourette syndrome. Bynoe's study is the first one to show a possible role of Toxo in Alzheimer's. This study might be the beginning of a conversation that brings awareness about the long-term impact of infections on brain health.

*-Luisa Torres, Postdoctoral Researcher in Microbiology & Immunology*

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