TOXO and JERRY

About cats, mice and behaviour-changing parasites

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The Science Communication Competition is now in its eighth year. As in previous years, it aims to find young talented science writers and give them the opportunity to have their work published in *The Biochemist*. In 2015, a new branch of the competition was launched to include video entries. Overall this year's competition attracted 74 entries and these were reviewed by our external panel of expert judges. The first prize in the written category was awarded to Victoria Bolton from the University of Glasgow, whose article is presented here; the winner of the video category was Jirayu Tanprasertsuk from Tufts University. Jirayu's winning video can be viewed at bit.ly/scicommvid2018.

One day, Jerry the small and clever mouse from the cartoon series "Tom and Jerry" stopped outsmarting the cat, Tom. Instead, Jerry no longer felt that Tom was his enemy. He felt an irresistible attraction towards Tom and how he smelt. Shortly after, Tom took his chance. Jerry ended up on Tom's plate, seasoned with salt and pepper and topped with mint sauce. Tom had Jerry for supper and lived happily ever after. THE END.

Imagine this was the end to an episode of "Tom and Jerry". That's the moment when you would probably say: "What is happening? Something is up!"

And you would be right. Something is up. Jerry is infected with a mind-controlling parasite called *Toxoplasma gondii*.

But what is *Toxoplasma gondii*? And how did Jerry become infected?

Toxoplasma gondii is a small parasite, about 40–400 times smaller than a small grain of sand. It can live in cells of any warm-blooded animal like a mouse, rabbit, your pet cat or us humans. *Toxoplasma*'s journey into Jerry begins in the gut of a cat like Tom, who is infected with *Toxoplasma gondii*. Tom, the cat and any other cat-like animal (e.g. tiger) are Toxoplasma's definitive host. This means Tom is Toxoplasma's home base: the place it must always come back to.

Tom, the cat, sheds small, round structures called oocysts in his stool. These structures have a very thick and protective wall, which protects them from extreme conditions in the outside world, just like the walls of your house protects you from the cold in winter. Like this, the oocysts can stay in the environment for a long time and mature.

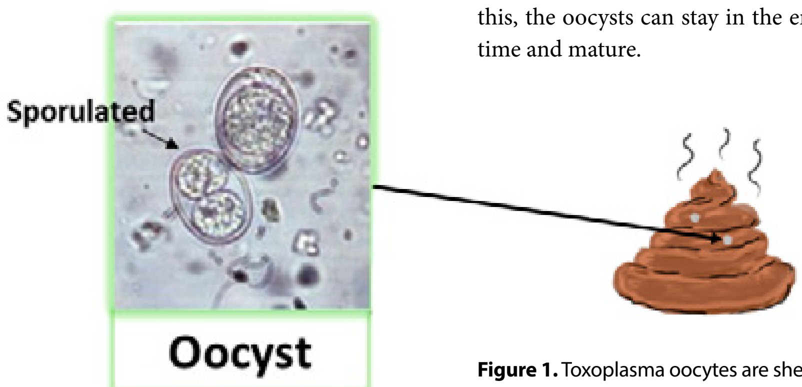

Figure 1. Toxoplasma oocytes are shed in cat faeces
Image of the oocyst is taken from fwfx.info/toxoplasma-gondii-egg.html

Jerry, or any other mice and small animals which cats feed on, are intermediate hosts. This means that they are a temporary home or place *Toxoplasma* visits and needs for its personal development, as it cannot stay at home all the time. Intermediate hosts like Jerry become infected because they accidentally take up *Toxoplasma*'s mature oocysts with their food.

After Jerry has consumed these small, round structures, they change their form to adapt to their new environment. It's very much like when you come in from outside on a winter's day wearing a thick jacket and enter a well-heated room. You change or undress as you do not need the thick warm clothes inside. Similarly, once inside, *Toxoplasma* gets rid of the structure with the thick protective wall; it changes into a small, drop-shaped structure called a tachyzoite.

Toxoplasma now has a mission. In order to thrive and survive, the parasite needs to get inside a cell. Sadly, for *Toxoplasma*, cells have a barrier around them called the 'cell membrane' that protects them like a wall around a castle.

Luckily, its new form – the tachyzoites – possess small sacks and structures called micronemes, dense granules and rhoptries inside, which contain molecules that help the parasite to move, invade and survive once inside the cell. These molecules are *Toxoplasma*'s personal set of aces up its sleeves, which it can shake out to win whenever they are needed.

Using some of these, tachyzoites can form a machinery called a glideosome that acts like a motor with which they can glide along the surface of the cell like a tank. With the force generated by the glideosome and some extra help of more *Toxoplasma* molecules, called AMA-1 and RON, which form a hoop called a moving junction, the parasite moves forward, front end first through the hoop and invades the cell. Toxoplasma then multiplies and lives happily inside the cell.

All very easy, *Toxoplasma*, right? Well…Jerry's immune system does not like to see this invader. It activates its alarm bells and sends its defence army of killer T-cells, whose function it is to sacrifice the infected cells and kill *Toxoplasma*. Since Jerry's army of defending cells sets out to kill, *Toxoplasma* chooses to withdraw from the battlefield. It creates small structures, called tissue cysts or bradyzoites where it can hide in the muscle or brain.

The brain is a special site. Not only because it is the control centre of our body, but also because most immune cells (cells that defend our body from 'invaders' like *Toxoplasma*) have restricted access to the brain. Thus, by hiding in the brain, *Toxoplasma* makes another smart move as most immune cells will not come looking for the parasite there. It's like laying low in a place with little surveillance, not creating too much uproar after you robbed a bank to avoid the attention of the police.

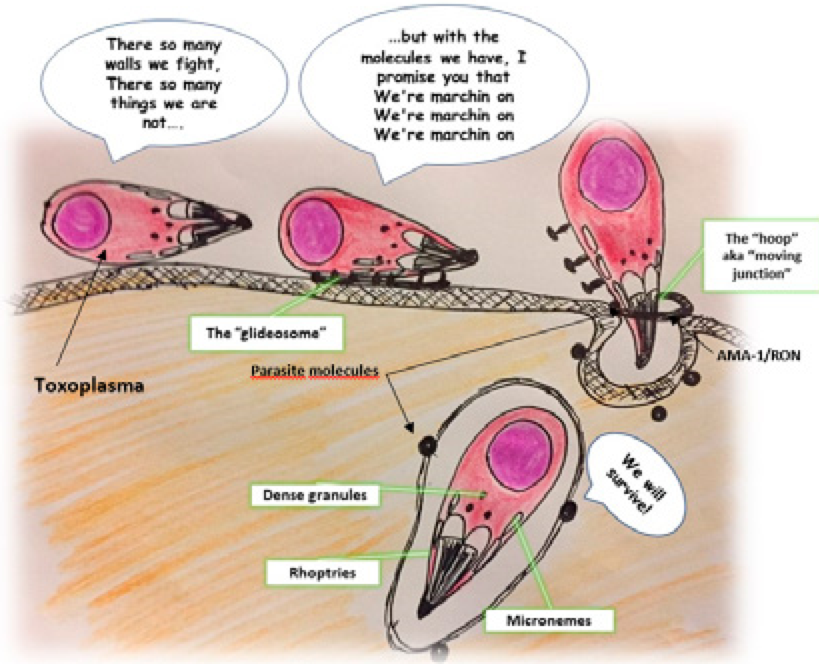

Figure 2. Parasite invasion into cells involves many parasite-secreted proteins

What happens next on *Toxoplasma*'s journey is very interesting. Mice like Jerry who have been infected for a while with Toxoplasma change their behaviour. Any other mouse would avoid cats like Tom and their smell. In contrast, Jerry, who is infected with *Toxoplasma* does not avoid Tom or Tom's smell, but instead becomes attracted to the scent. Jerry even develops an interest in sniffing Tom's pee (oh dear). This makes Jerry an easy meal for a cat like Tom.

But how does *Toxoplasma* make Jerry act like that?

The exact mechanism of how *Toxoplasma* changes Jerry's behaviour remains to this day unknown, but there are several possible explanations:

One explanation is that Jerry's behaviour could be changed because *Toxoplasma* forms cysts in the brain areas that control Jerry's feelings of fear, his senses and his decision making. That way, *Toxoplasma* could simply mix up their normal function, just like an uninvited, hostile intruder into a headquarter or the parliament would. The outcome being Jerry losing his fear of Tom and his smell.

Another possibility is that some of *Toxoplasma*'s molecules are involved in changing Jerry's behaviour. Two molecules of *Toxoplasma*, called AAH1 and AAH2, are very similar to a human molecule that is involved in making dopamine. Dopamine is a chemical that can be found in our brain and is involved in the creation of 'reward' and 'pleasure' feelings. One could say that dopamine is the molecule of lust, motivation and addiction. By producing molecules that are similar to those involved in making more of the chemical dopamine, *Toxoplasma* may increase dopamine levels in Jerry's brain, thereby changing Jerry's behaviour in a way that he is attracted instead of repelled by the smell of Tom. Indeed, scientists have found that the areas around the structures *Toxoplasma* forms in the brain contain a lot of dopamine.

A third possibility involves the male sexual hormone testosterone, a hormone responsible for sexual and risky behaviour. It is the hormone that changes your calm husband, friend, boyfriend or brother into a roaring Neanderthal who thinks he can take it up with the whole world during a Sunday football match. This hormone has been found at increased levels in male rats infected with *Toxoplasma*.

Thus, as a result of increased testosterone levels in his blood, Jerry may become more daring and think he can take it on with a cat. Moreover, since testosterone increases sexual behaviour, Jerry even may become attracted by the cat's smell, like he would be attracted by a charming mouse lady.

By whatever mechanism *Toxoplasma* changes Jerry's behaviour, Jerry ends up as Tom's supper. Jerry's demise is good for *Toxoplasma*, because Jerry was just a temporary home for *Toxoplasma* and it needs to get back to its definitive host: the cat, Tom. The eternal cycle of cats, mice and mind-controlling parasites is completed.

Does *Toxoplasma* also change human behaviour?

But *Toxoplasma* is not only a parasite of mice and cats but can also infect us humans. In fact, one in three people worldwide are infected with this parasite. Humans become infected by the consumption of undercooked meat of an infected animal or food or water that has become contaminated with cat faeces.

Since we are unlikely to be the meal of a cat or tiger (unless we are the adventurous type on a jungle safari), *Toxoplasma* lives within us inactivated as cysts in the muscle, heart, brain or eyes. Does that mean we have a preference for cat urine now? Not necessarily. Some studies suggest that the parasite increases jealousy and the tendency to disrespect rules, while others point out a link between *Toxoplasma* infection and schizophrenia. Although you may think now that your jealousy is the result of 'advanced' parasite-mediated mind control, most studies have studied correlation, not cause-effect, limiting the extent to which we can conclude if the parasite changes our human behaviour. So, no reason to worry.

Nevertheless, *Toxoplasma* infection can have serious consequences: in pregnant women that become infected for the first time, *Toxoplasma* can be transferred from the mother to the unborn baby where it can cause serious birth defects.

While Jerry sadly cannot be saved, if you are not yet infected and you are planning to have a baby, you can minimise the risk of becoming infected by simple means like cooking your meat properly and washing your hands, fruits and vegetables. ■

Further reading

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