Extraordinary Tales

Parasites Hijacking the Minds of Hosts

Felix Bast

In the context of biology, parasites are organisms that typically associate with other organisms, their hosts, such that the hosts are damaged while the parasites are benefited. This non-mutual association is known as parasitism. Parasites do not form an evolutionarily distinct group; instead they are part of many different lineages. For example, there are parasites that are protozoa, plants, fungi and animals. Parasitology refers to the study of parasites, with an emphasize on protozoan (single-celled organisms that belong to Kingdom Protista) parasites. This article examines some of the parasites that cause behavioural changes in their host which help the perpetuation of the parasites; either their spread or their lifecycle completion. Specifically, the article examines the tactics of *Toxoplasma gondii*, lancet liver fluke, guinea worm, the influenza virus, and the parasitic wasp, which are by all means 'evolution's neurobiologists', and are indeed extraordinary in many aspects.

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Introduction

For many decades, an evolutionary biologist, Jaroslav Flegr, from Charles University in Prague, Czech Republic suspected that a single-celled protozoan parasite, *Toxoplasma gondii*, was doing extraordinary things to his own mind; taking it hostage, and tweaking neuronal connections and neurochemistry to get things done for the parasite. He could eventually prove his hunch [1]. What is more, according to recent estimates, half of the world's population – around 3.5 billion of us – have this tiny organism as a latent pathogen in our brain! Cat lovers beware; we get this parasite from cats [2].

Most of the protozoan parasites have a definitive host (the host

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that is required to complete its lifecycle), and an intermediate host – which is likely necessary for the completion of a few lifecycle stages of the parasite. For example, in case of *Plasmodium vivax*, the malarial protozoan, the definitive host is the *Anopheles* mosquito since the parasite completes its entire lifecycle in the mosquito itself. The intermediate host of *P. vivax* is a human being; the parasite causes malaria when it infects us. Why would this parasite infect us if we are optional in its lifecycle? Of course, this aids in the spreading the parasite to many individuals all at once. For example, one affected human being can serve as a giant 'bank' for these parasites; he or she will aid in the dissemination of this parasite to hundreds of other mosquitoes, of course, unknowingly. Remember that mosquito-to-mosquito infection of protozoan parasites is a relative rarity.

Toxoplasma gondii

In case of *T. gondii*, cats are the definitive host, as *T. gondii* can sexually reproduce only within cats. The parasite spreads from cats to its intermediate hosts – rats and humans – via the faecal–oral (faeces to mouth) route. In this mode of transmission, healthy animals ingest food contaminated with parasite-containing faeces. The faecal–oral route is common in a number of other infectious diseases affecting humans, including cholera and typhoid fever.

It has been known since the 1920s that *T. gondii* causes toxoplasmosis in humans. Toxoplasmosis is typically a mild asymptomatic disease, with flu-like symptoms in some patients. However, the parasite can cross the placenta to infect the fetus that results in congenital toxoplasmosis – a potentially fatal disease for fetuses, leading almost certainly to stillbirth if not treated. This is the reason pregnant women are told to avoid cleaning cat litter boxes. We also acquire this parasite by eating undercooked meat and unclean fruits and vegetables that might have been contaminated with cat faeces. Toxoplasmosis is a major threat to people with reduced immunity, including AIDS patients and those who take immunosuppressant medicines after transplantation (for example, kidney transplantation). Healthy individuals can quickly fight off

this parasite after the mild infection and subsequently, the parasite becomes latent and 'resides' in the brain lifelong.

Interestingly, as Flegr suspected, these parasites are not merely living in the brain, but are also doing some nasty things. Before expounding on what happens in humans, let us consider how the parasite affects rats – yet another of its intermediate hosts. It is usual for rats to avoid cats, as cats prey on them. Rats having *T. gondii* in their brain on the other hand are weird, in that they become attracted to cats! Amazingly, the parasite hijacks the rat's brain such that its behavior is affected. Rats become allured to feline urine and body odor, a behavior dubbed as 'fatal feline attraction'. Research has revealed that this appeal is specific to feline odor, not for odors of any other predators of rats, such as the mink. Instead of running away briskly from cats, the affected rats behave boldly in front of cats, and they grab the attention of cats. Of course, this is suicidal for the rat, but the parasite has already hijacked its mind. Why would the parasite need the cats to kill its host? To get into the cats for completing its lifecycle, of course. See how smart *T. gondii* are!

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Recent research has revealed exactly how *T. gondii* affects the behavior of rats. This is achieved, in part, through epigenetic remodeling in neurons – the dynamic modification of chromosomal structure so that transcription (transfer of information from DNA to mRNA) is affected, ultimately controlling the gene expressions [3]. This occurs at an almond-shaped region in the brain, amygdala (*Figure* 1), which is involved in decision-making, memory, emotional reactions and cognitive response. The amygdala is a very primitive region; indeed all vertebrates have it, including amphibians, reptiles, birds, and mammals.

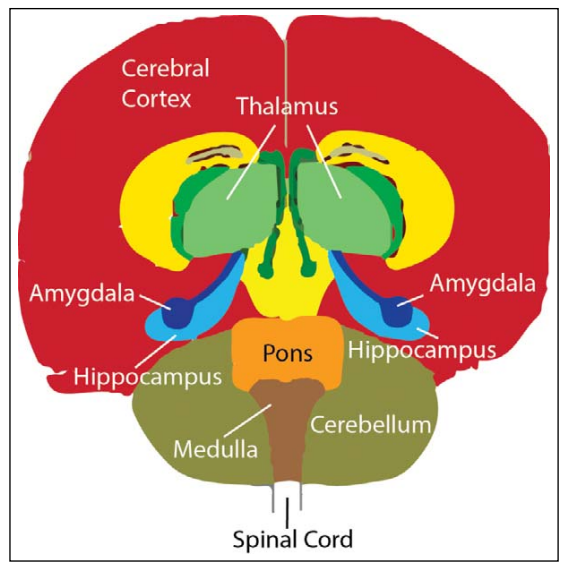

Figure 1. Location of amygdala inside human brain. Designed by author in Adobe Illustrator.

After decades-long investigations, Flegr published a well-cited paper in 1994 reporting

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that men carrying the *T. gondii* latent infection are more likely to disregard rules and to become excessively jealous and suspicious [4]. He subsequently reported that cognitive response times become longer (responses become delayed) for those who are affected by this pathogen. The cognitive response is extremely relevant in activities that demand quick response, like driving; if your response is delayed, you are more prone to accidents. His 2002 paper confirmed that it was twice more likely for those involved in traffic accidents, for having a prior infection with *T. gondii* [5].

A 2009 paper analyzed the genome of *T. gondii* and found that it had two genes coding for tyrosine hydroxylase [6]. Tyrosine hydroxylase is a known enzyme for the production of dopamine – a neurotransmitter in mammals. Apparently, the parasite does not need this enzyme, as dopamine has no effect on its 'brain', which is nonexistent. Dopamine plays roles in cognition, motivation, apprehension and gratification, and this might hint at the many ways *T. gondii* hijacks our mind. Research has confirmed that dopamine levels in infected rats were significantly higher than in the uninfected. Drugs such as haloperidol that act against the production of dopamine are able to ward off symptoms associated with the 'fatal feline attraction'syndrome. Increased dopamine in humans is linked to psychotic diseases like schizophrenia, and haloperidol is, in fact, being used to treat the disease. Research has also revealed that people infected with *T. gondii* are more likely to develop schizophrenia [7, 8].

An Indian-origin scientist Ajai Vyas at Nanyang Technological University, Singapore has recently come up with yet another interesting finding of *T. gondii* [9]. Vyas found that this parasite resides in the testes of rats, and is passed on to the females during copulation, confirming that toxoplasmosis is a sexually transmitted disease as well [10]. He found that more than half of their offspring got the parasite this way. The research also revealed that *T. gondii* increases testosterone levels in male rats infected with it. Testosterone is the male sex hormone, and increased levels of this hormone result in increased libido. Research has

also revealed that the male rats with toxoplasmosis not only breed at a faster rate, but also are judged to be far more attractive by the female rats. Having got the testosterone rush, these rats become sexually aroused by feline urine smell, and they 'get caught in the middle of the act' by the cats, completing the lifecycle of parasites! See how amazing *T. gondii* are! They are evolution's neurobiologists; by manipulating mammalian brains and body, they have evolved ways to alter behavior, thus possessing our minds.

They are evolution's neurobiologists.

Flegr's recent research confirms analogous behavior in humans as well [11]. Males with toxoplasmosis had significantly higher testosterone levels and had a higher probability of being judged as sexually attractive by females. In the light of studies in rats, this behavioral manipulation will enable the parasites to spread between humans via sexual intercourse. However the question remains: what would be the probable function of altered cognitive response times? Why would the parasite need us to be killed in traffic accidents? Unlike rodents, we are not a prey for cats to complete its lifecycle. Flegr's 2011 paper confirms that humans affected with toxoplasmosis also exhibit a 'fatal feline attraction'; they are more attracted to cats, although the attraction might not be fatal [12]. This paper attracted such wide media attention in the West that a name was coined for the human behavioral disease, 'crazy cat lady syndrome'. Stereotypical cat-lovers in the West are mostly women, especially middle-aged spinsters[1].

[1] Having kept cats for most of my early life, I also strongly suspect that I have *T. gondii* lodged in my mind. At one point in my life, I was very attracted to cats. After browsing through British Council Library in Chennai, I came across books on ancient Egyptian cat goddess Bast (or Bastet). So much was my feline attraction that I eventually decided to change my name from a traditional hindu brahmin name (Vadakke Madam Sreejith) to an irreligious (philosophers Bertrand Russell and Voltair – who changed his name to an anagram – were my role models!) archetypal feline name (Felix Bast). I considered Felix as the best first name for me, resembling *Felis* – the genus of cats, and because of the famed 'Felix the Cat' character. I now strongly suspect that it was *T. gondii* benignly residing in my brain that did all those decision-makings! Of course, I still love cats, albeit a little less than I love my daughters and wife!

Lancet Liver Fluke

Toxoplasma gondii is not the only parasite that induces behavioral changes in the host for its advantage. Another well-known parasite is the flatworm lancet liver fluke (*Dicrocoelium dendriticum*) (*Figure* 2), a parasite of the cattle [13]. When it infects ants – its intermediate host – it manipulates the behavior of the ants such that instead of their usual tendency to avoid blades of grass and walking towards the ground, they climb the blade. The ants cling to the apex of grass blades with their jaws so tightly

Figure 2. Lancet liver fluke (*Dicrocoelium dendriticum*). Image credits: http://bestwalle.mobi/

clenched that they cannot even release their own bite, thereby easily becoming the prey of cattle that graze on the grass. Cattle are the parasite's definitive host, as they enable them to reproduce sexually, thus completing their lifecycle.

Guinea Worm

Another example is the nematode guinea worm (*Dracunculus medinensis*) (*Figure* 3), that cause a skin disease in human called dracunculiasis [14]. A person is infected when he or she drinks water containing water-fleas that have been infected with the guinea worm larvae. In the first year, infected persons show no symptoms, as the parasite produces opiate alkaloids including morphine that down-regulates immune responses and pain signaling in hosts [15]. After a year, they get an itchy and very painful subcutaneous lesion, especially on the legs, prompting the patients to wash the lesions regularly. By washing the lesions, the larvae of guinea worm gets released from the skin, and finally it can reach back to the water bodies, for infecting the water fleas!

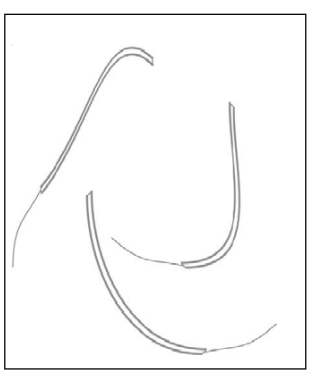

Figure 3. Guinea worm *(Dracunculus medinensis)*. Designed by author in Adobe Illustrator.

The Influenza Virus

Another example is the influenza virus, the causative agent of influenza and flu. Research has revealed that people who had taken an annual flu shot that contained an attenuated form of the virus, were significantly more sociable in the four days following the vaccination than in the four days preceding it. Though the viruses contained in the vaccine were attenuated (that cannot cause disease), they probably elicited behavioral changes in a way similar to the responses elicited by virulent (disease-causing)

viruses in the patients [16]. Obviously, making the hosts more sociable is a good thing for the virus, as it enables them to spread quickly.

Figure 4. Parasitic wasp *Polysphincta gutfreundi*. Image credits: Smithsonian Institution, USA

Polysphincta Wasps

Kidnapping the host's mind is the tactic of parasitic wasp (insect) *Polysphincta gutfreundi* (*Figure* 4) as well [17]. The wasp grabs hold of an orb-weaver spider (*Araneidae* family) and attaches a tiny egg to its belly. The egg matures to worm-like larva that releases chemicals which alter the behavior of the spider. Instead of weaving the familiar spiral web, the infected spider spins its silk thread into an intricate pattern (*Figure* 5) that will hold the cocoon in which the larva matures. What is more, the infected 'zombie' spider even weaves distinct geometric patterns into the web, camouflaging the cocoon from the wasp's predators.

Ichneumon Wasps

In a sense, the Ichneumon wasps (*Figure* 6) are truly legendary. They are Nature's ultimate barbaric anesthetists – the major

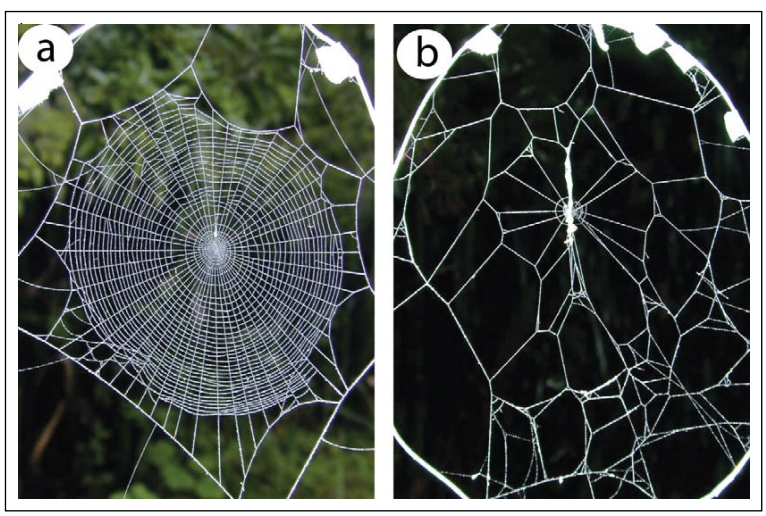

Figure 5. Contrast between geometric patterns of the webs of orb-weaver spider *Allocyclosa bifurca*. **a**. Normal pattern. **b**. Pattern after infection with parasitic wasp. Image credits: Smithsonian Institution, USA.

Figure 6. Ichneumon wasp's larvae bursting out of the host caterpillar [18].

preoccupation of Victorian theodicy. These wasp parasites paralyze, but not kill, their hosts – the caterpillars – before laying eggs on the latter's body. The wasp, with the precision of a meticulous anesthetist, carefully stings and thereby paralyses each nerve ganglion of the caterpillar. The larvae mature inside the hijacked caterpillar and devour its internal organs in such a surgical order that the most vital organs, heart and the nervous system, are consumed last to make the host live as long as possible.

These same wasps bemused Darwin during his visit to Australia, where they are commonly found. In a letter addressed to his friend, Asa Gray, dated 22nd May, 1860, Darwin wrote: "I cannot persuade myself that a beneficent and omnipotent God would have designedly created the *Ichneumonidae* with the express intention of their feeding within the living bodies of caterpillars". Richard Dawkins in his latest book, *The Greatest Show on Earth*, observed less euphemism while referring to the designer of these wasps, if any, as "sadistic bastard" [18].

Conclusion

How these parasites have evolved to elicit behavioral changes in the host is one of the most fascinating subjects in biology, yet presumably very complex to understand. There might be several parasites acting together; their labyrinthine ecological niche within our human brain might be the ultimate controller of the human behavior. In the light of these mind-hijacking parasites, seemingly simple quotidian chores like gardening, cleaning the litter

They are Nature's ultimate barbaric anesthetists.

box, or bathing suddenly get more attention, and allow us to appreciate the artistry of this magnificent process that is evolution.

Suggested Reading

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