

Toxoplasma gondii: Parasite of the Mind?

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None are more hopelessly enslaved than those who falsely believe they are free.

-Johann Wolfgang von Goethe

Mind control remains, for most, the preserve of science fiction; however, it appears to be a very real phenomenon in nature. Many parasites have been observed to modulate the behaviour of their hosts to favour completion of their life cycles [1]. Amongst these is the protozoan parasite *Toxoplasma gondii*, which can infect virtually any warm-blooded animal. *T. gondii* has been shown to alter the behaviour of the rodents it infects. Given that this parasite infects up to half of the UK population at some stage and 30% of the world's population, its potential role in influencing our behaviour is an active area of research, uncovering to what extent we really are the masters of our own minds [2, 3].

T. gondii has a complex life cycle consisting of two phases: sexual reproduction, which it only undergoes in the cat, and asexual reproduction, which it undergoes in its other hosts, such as the rat. In contrast to other related parasite groups such as the Plasmodia, whose members cause malaria, *T. gondii* infects most people asymptotically and only causes serious disease in the immunocompromised (e.g. AIDS patients) or in the foetus when the mother becomes infected during pregnancy [4]. Like most parasites, *T. gondii* has acquired many morphological adaptations to enable it to survive and replicate in its hosts but it may also have the ability to manipulate their behaviour to its own ends. Particular attention has been devoted to its alteration of the behaviour of infected rats and mice but there is some evidence to suggest it may also influence human behaviour.

Rats have an innate aversion to the odour of their natural predator, the cat. This is even observed in laboratory rats that have not had contact with cats for several hundred generations. However, rats infected with *T. gondii* do not show the same fearful responses to cat odours but, in fact, are attracted to them [5]. Such an adaptation is highly desirable for the parasite as it increases the probability of the rat being caught and eaten by the cat, allowing it to complete its life cycle. Clearly, some complex neurobiological manipulation must underlie this dramatic alteration of a hard-wired behaviour.

Chronic infection with *T. gondii* is characterised by the formation of cysts in the host's brain. The cysts are prevalent in limbic areas of the brain, which modulate emotional processes. This is in keeping with the idea that *T. gondii* could be influencing host behaviour [6]. One such area where cysts are prevalent is the amygdala, an almond-shaped group

of nuclei associated with fear conditioning. The inhibition of transmission between neurons in the amygdalae of rats has been shown to reduce fear of cats in a similar way to *T. gondii* infection [5]. However, it is becoming clear that *T. gondii* acts in a much more subtle manner than by a general blockade of neurotransmission. The change in the response to cat odours observed in *T. gondii* infected rats has been shown to be highly specific, leaving many other fear-related behaviours associated with the amygdala intact [7].

This is only half the story as *T. gondii* not only ablates the aversive reaction to cat odours in rats but also makes them attractive. A working hypothesis is that *T. gondii* hijacks the brain's reward pathway, making cat odours seem attractive. It has been shown that *T. gondii*'s genome contains two genes coding for tyrosine hydroxylase, an enzyme involved in the synthesis of dopamine. Dopamine is the neurotransmitter believed to underlie the reward pathway in the brain. It is postulated that *T. gondii* can make cat odours seem attractive by producing this enzyme and, thus, increasing dopamine levels in infected rodents' brains [8]. Drugs that block dopamine receptors to infected rats abolishes their attraction to cat

urine, further supporting this idea [9]. The fact that these drugs are currently being used to treat schizophrenia might suggest a link between the parasite and human affective disorders.

While there is a significant body of evidence for *T. gondii* modulating the behaviour of

infected rodents, whether it is having an effect on humans remains controversial. It is naturally difficult to accept that something as seemingly simple as a single-cell organism could manipulate something as complex as human behaviour. However, there is emerging evidence to suggest that infection with *T. gondii* may not be without any behavioural effects in humans but this is still very much open to debate. For example, it has been shown that there is an increased prevalence of antibodies against *T. gondii* (an indication of *T. gondii* infection) in individuals with schizophrenia [10]. One of the leading hypotheses in the neurobiology of schizophrenia is that the condition results from an elevation of dopamine levels, which is consistent with the fact that *T. gondii* has two genes encoding a key enzyme in the dopamine synthesis pathway and that drugs used to treat schizophrenia can reverse *T. gondii*-associated behaviour in rats [8, 9]. Infection has also been associated with a 2-3 times greater risk of being involved in a car accident and at recent study has suggested that there is an increased suicide rate amongst post-menopausal women infected with *T. gondii* [11, 12].

The *T. gondii* 'story' has captured the imagination of some in the media and many claims have already been made about the nature and extent of the effects of its infection. The

“ There is some evidence to suggest it could also influence human behaviour and predispose to disorders such as schizophrenia ”



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title of a report on *T. gondii*, 'Cat Parasite affects everything we feel and do', is an example of a story covering the parasite [13]. Other more specific claims include a possible association between *T. gondii* infection and certain personality traits in individuals, willingness to take risks, major cultural differences on the planet, the sale of motor cycles, and even the likelihood of a country winning the World Cup [14].

With so many behaviours being attributed to *T. gondii*, it is important to emphasise that much is still unclear about the extent, if any, to which *T. gondii* can influence human

behaviour. The subtlety of its actions observed so far has led scientist Robert Sapolsky to say that *T. gondii* "knows more about the neurobiology of anxiety and fear than 25,000 neuroscientists standing on each other's shoulders" [15]. By studying *T. gondii*, we could gain an insight not only into how this remarkable parasite modulates host behaviour but also into the neurobiology of fear and other conditions. ■

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References:

- Listverse [<http://listverse.com/>] 10 Fascinating Cases of Mind Control Available from <http://listverse.com/2009/07/29/10-fascinating-cases-of-mind-control/>
- NHS [www.nhs.uk] Toxoplasmosis Available from <http://www.nhs.uk/conditions/Toxoplasmosis/Pages/Introduction.aspx>
- Montoya JG, Liesenfeld O. Toxoplasmosis. *Lancet*. 2004 Jun 12;363(9425):1965-76. Available from <http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2804%2916412-X/fulltext>
- Despommier; Gwadz; Hotez; Knirsch Parasitic Diseases, Fifth Edition 2005
- Berdoy M, Webster JP, Macdonald DW. Fatal attraction in rats infected with *Toxoplasma gondii*. *Proc. Biol. Sci.* 2000;267:1591-1594. Available from <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1690701/?tool=pubmed>
- Melzer TC, Cranston HJ, Weiss LM, Halonen SK. Host Cell Preference of *Toxoplasma gondii* Cysts in Murine Brain: A Confocal Study *J Neuroparasitology*. 2010;1. pii: N100505. Available from <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3103221/?tool=pubmed>
- Vyas A, Kim SK, Giacomini N, Boothroyd JC, Sapolsky RM. Behavioral changes induced by *Toxoplasma* infection of rodents are highly specific to aversion of cat odors *Proc Natl Acad Sci U S A*. 2007 Apr 10;104(15):6442-7. Epub 2007 Apr 2. Available from <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1851063/?tool=pubmed>
- Gaskell EA, Smith JE, Pinney JW, Westhead DR, McConkey GA. A Unique Dual Activity Amino Acid Hydroxylase in *Toxoplasma gondii* PLoS One. 2009;4(3):e4801. Epub 2009 Mar 11. Available from <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2653193/?tool=pubmed>
- J.P Webster, P.H.L Lamberton, C.A Donnelly and E.F Torrey. Parasites as causative agents of human affective disorders? The impact of anti-psychotic, mood-stabilizer and anti-parasite medication on *Toxoplasma gondii*'s ability to alter host behaviour *Proc. R. Soc. B* 2006 273, 1023-1030 Available from <http://rsob.royalsocietypublishing.org/content/273/1589/1023.full.pdf>
- da Silva RC, Langoni H. *Toxoplasma gondii*: Host-parasite interaction and behavior manipulation. *Parasitol Res*. 2009 Oct;105(4):893-8. Epub 2009 Jun 23. Available from <http://www.springerlink.com/content/k7566654742p6512/>
- Flegr J, Klose J, Novotná M, Berenreitterová M, Havlíček J. Increased incidence of traffic accidents in *Toxoplasma*-infected military drivers and protective effect RhD molecule revealed by a large-scale prospective cohort study. *BMC Infect Dis*. 2009 May 26;9:72. Available from <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2692860/?tool=pubmed>
- Ling VJ, Lester D, Mortensen PB, Langenberg PW, Postolache TT. *Toxoplasma gondii* Seropositivity and Suicide Rates in Women. *J Nerv Ment Dis*. 2011 Jul;199(7):440-4.
- abc News [www.abcnews.com] Cat parasite affects everything we feel and do. Available from <http://a.abcnews.com/Technology/DyeHard/story?id=2288095&page=1>
- Next Nature [www.nextnature.net] The Cat Parasite that Sells Motorcycles. Available from <http://www.nextnature.net/2011/02/the-cat-parasite-that-sells-motorcycles/>
- Edge Foundation, Inc [www.edge.org] TOXO: A Conversation with Robert Sapolsky. Available from http://www.edge.org/3rd_culture/sapolsky09/sapolsky09_index.html
- Watanabe, Chika [image on the Internet]. Available from: <http://www.flickr.com/photos/chikawatanabe/3626066979/> under CC-BY 2.0 license.