“Behavioral changes induced by *Toxoplasma* infection of rodents are highly specific to aversion of cat odors”

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Parasite "Brainwashes" Rats Into Craving Cat Urine, Study Finds

Fatal attraction in rats infected with Toxoplasma gondii

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Rats, cats, people and parasites: the impact of latent toxoplasmosis on behaviour

Joanne P. Webster*

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

J. P. Webster¹,*;†, P. H. L. Lamberton¹,†, C. A. Donnelly² and E. F. Torrey³
Parasites modifying behaviors...

- Rabies virus
- “Suicidal” grasshoppers infected with the hairworm *Spinochordodes tellinii*
- Some nematodes infect crustaceans
- Species of pinworm and rodents
Toxoplasma gondii transmission

High Prevalence:

- 45% cats
- 20–60% wild rodents
- 13.4–66.7% wild birds
- 22–84% humans

www.roche.com/pages/facets/2/toxoplasma.jpg
Tachyzoites

Oocysts

Luciferase and GFP

Subjects

Long evans rat

8 wks, multipurpose

Balb/c mice

7 wks, abs

http://www.iar.or.jp/shodobutsu/le_rat/index.html
Health status of control and infected animals were comparable.
Acute to chronic infection

Fig. 1. Infection caused a transient increase in luminescent signals emanating from parasites. The series of images reflects the spread of luminescent signal at successive days after infection. Photon flux is coded by a range of pseudocolors (lowest, blue; highest, red).

Behavioral expts 4-5wks after infection, no sickness behavior 30d post infection
Infection abolished aversion to bobcat urine in rats, instead producing an attraction.
Infection abolished aversion to bobcat urine and cat collar in mice. Increased the ratio of occupancy in the bobcat quadrant vs. the rabbit quadrant.
Infection did not influence locomotion & anxiety in an open field arena in rats

Fig. 4. Infection did not affect anxiety-like behavior of rats in the open-field
Infection did not affect spatial memory in rats

Table 1. Infection did not affect spatial memory in rats as measured in the Morris water maze

<table>
<thead>
<tr>
<th>Mouse</th>
<th>Occupancy in target quadrant, %</th>
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<tbody>
<tr>
<td></td>
<td>Day 0</td>
</tr>
<tr>
<td>Control</td>
<td>34.7 ± 6.2</td>
</tr>
<tr>
<td>Infected</td>
<td>32.6 ± 1.3</td>
</tr>
</tbody>
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Data show the preference for the target quadrant during the probe trial conducted immediately after and 1 day after training.
Morris rat maze

http://www.ratbehavior.org/RatsAndMazes.htm
Infection did not affect spatial memory

Fig. 9. Infection did not affect spatial memory in rats measured in Morris water-maze. (A) Latencies to reach a
Infection did not influence fear conditioning or its extinction in rats

Fig. 5. Infection did not affect freezing during various phases of fear
Infection did not affect neophobia toward food of novel scent in mice.
Localization of tissue cysts in the brain

Wide range coronal levels in brain
Mainly in amygdala

Cysts in brain regions for defensive behaviors
Authors Conclusion

- Replicated the findings
- Effects of infection are highly specific
- Other behaviors not affected
- In chronically infected rats, parasite cysts were randomly distributed over the entire brain.
- Observed that cyst density in amygdalar structures was 2-fold higher than on nonamygdalar structures
Possible Explanations...

• “Manipulation hypothesis”
• Host manipulation, parasite enhances its own transmission by altering host behavior. ‘the manipulation hypothesis’.
• Implication of parasite evolution aimed at host manipulation, rather than an accidental side effect of infection.
• Questions include 1)behavioral modifications adaptation or merely a side effect of parasite host interactions. 2) Sickness behaviors and 3) are behavioral changes following infection inherited from ancestors (phylogeny)
• Biggest problem is difficult to elucidate whether a behavioral change following infection is a non-adaptive
Possible explanations

- Support Manipulation hypothesis
- Dedicated neurocircuitry mediating antipredator defensive behaviors related to connections between the amygdala and hippocampus
- Possibly a set of neural mechanism or substrates that are dedicated only to the processing of cat odors is affected. *T. gondii* or infected cells produces substances
- Subtle tropism, *T. gondii* infection selectively localizes to certain areas of brain more sensitive to neuronal damage
- Perhaps infection causes neuromodulatory changes (systems dispensing different neurotransmitters like dopamine)
Brain slugs?

http://sciencefictionbiology.blogspot.com/2006/10/parasites-that-control-behavior.html
Questions?

http://katenhond.blog.nl/kat/2007/04/10/de-vreemde-geheimen-van-toxoplasma
Parasite manipulation of host behaviors, why, how?

- Presumption: parasites manipulate the behavior of their hosts to increase the probability of transmission to another host—prevailing hypothesis.
- Are we too quick to assume that behavioral changes following infection are adaptive for the survival and reproduction of the parasite? Yes.
- Not all behavioral modifications following infection are mediated by parasites and not all behavioral modifications have evolved to increase the reproductive success of the parasite.
- Questions include 1) are behavioral modifications following infection an adaptation or merely a side effect of parasite-host interactions. 2) are behavioral changes following infection mediated by the host to overcome infection eg. Sickness behaviors and 3) are behavioral changes following infection inherited from ancestors (phylogeny).
- Biggest problem is difficult to elucidate whether a behavioral change following infection is a non-adaptive side-effect of infection or not. Several operational definitions for the term “by product of infection includes 1) that behavioral changes are pathological consequences of infection that are not adaptive to either the host or the parasite 2) that the behavioral modification is coincidentally beneficial to both the host and parasite 3) the behavioral change is just a fortuitous payoff of another adaptation. Difficult to test these hypotheses.