Short Communication

Does *Toxoplasma* infection increase sexual masochism and submissiveness? Yes and no

Jaroslav Flegr

Division of Biology, Faculty of Science, Charles University, Vinicna 7, Prague 128 44, and National Institute of Mental Health, Klecany, 250 67, Czechia

Submitted: 13 February 2017

Accepted:

Key words: Toxoplasmosis; violence; parasitism; manipulation; sexual behaviour; BDSM; epigenetics; big data; multivariate statistics; complex systems.

Correspondence to:

Jaroslav Flegr

Email: flegr@cesnet.cz

Abstract

The parasite *Toxoplasma* needs to get from its intermediate hosts, e.g. rodents, to its definitive hosts, cats, by predation. To increase the probability of this occurrence, *Toxoplasma* manipulates the behavior of its hosts, for example, by the demethylation of promoters of certain genes in the host's amygdala. After this modification, the stimuli that normally activate fear-related

circuits, e.g. the smell of a cat, or smell of leopards in chimpanzee, start to additionally co-activate sexual arousal-related circuits in the infected rodents. In humans, the increased attraction to masochistic sexual practices was recently observed in a study performed on 36,564 subjects. Here I show that lower rather than higher attraction to sexual masochism and submissiveness among infected subjects is detected if simple univariate tests instead of multivariate tests are applied to the same data. I show and discuss that when analyzing multiple effects of complex stimuli on complex biological systems we need to use multivariate techniques and very large data sets. We must also accept the fact that any single factor usually explains only a small fraction of variability in the focal variable.

TEXT

The protozoan parasite *Toxoplasma* is transmitted from intermediate hosts (any warm-blooded animal) to its definitive hosts (any feline species) by predation. *Toxoplasma* is one of many parasites that are known to manipulate the behavior of their hosts to increase their chances of effective transmission from infected to noninfected individuals.[1] The most spectacular behavioral effect of *Toxoplasma* in rodent hosts is the so-called fatal attraction phenomenon (FAP) – the change of native fear of the smell of cats into attraction to their scent among individuals infected by the parasite.[2] *Toxoplasma* infects about one third of the human population. Many behavioral effects of *Toxoplasma* have been observed in humans, including the analogy of FAP. Infected men positively rate the attractiveness of highly diluted urine of cat, but not of four other animals, higher than noninfected controls.[3] The mechanism of FAP in rats is based on the demethylation of promotors of certain genes in amygdala. After this, the stimuli that normally activate fear-related circuits in amygdala begin to also activate sexual arousal-related circuits in the infected animals.[4,5] The mechanism is rather specific – the fear of smell of potential definitive hosts of *Toxoplasma*, for example the smell of domestic cats in

mice or smell of leopards in chimpanzee, is changed into the attraction, while of smell of other predators remains intact. [6,7] It is not clear, whether such mechanism helps to achieve desired specificity of FAP, or whether it is just a product of neuroanatomical constraints. Possibly, it is easier to achieve the co-activation of the fear-related and the sexual arousal-related circuits by specific stimuli in a mammal brain than to achieve an inhibition of the activation of the fear-related circuits by such stimuli.

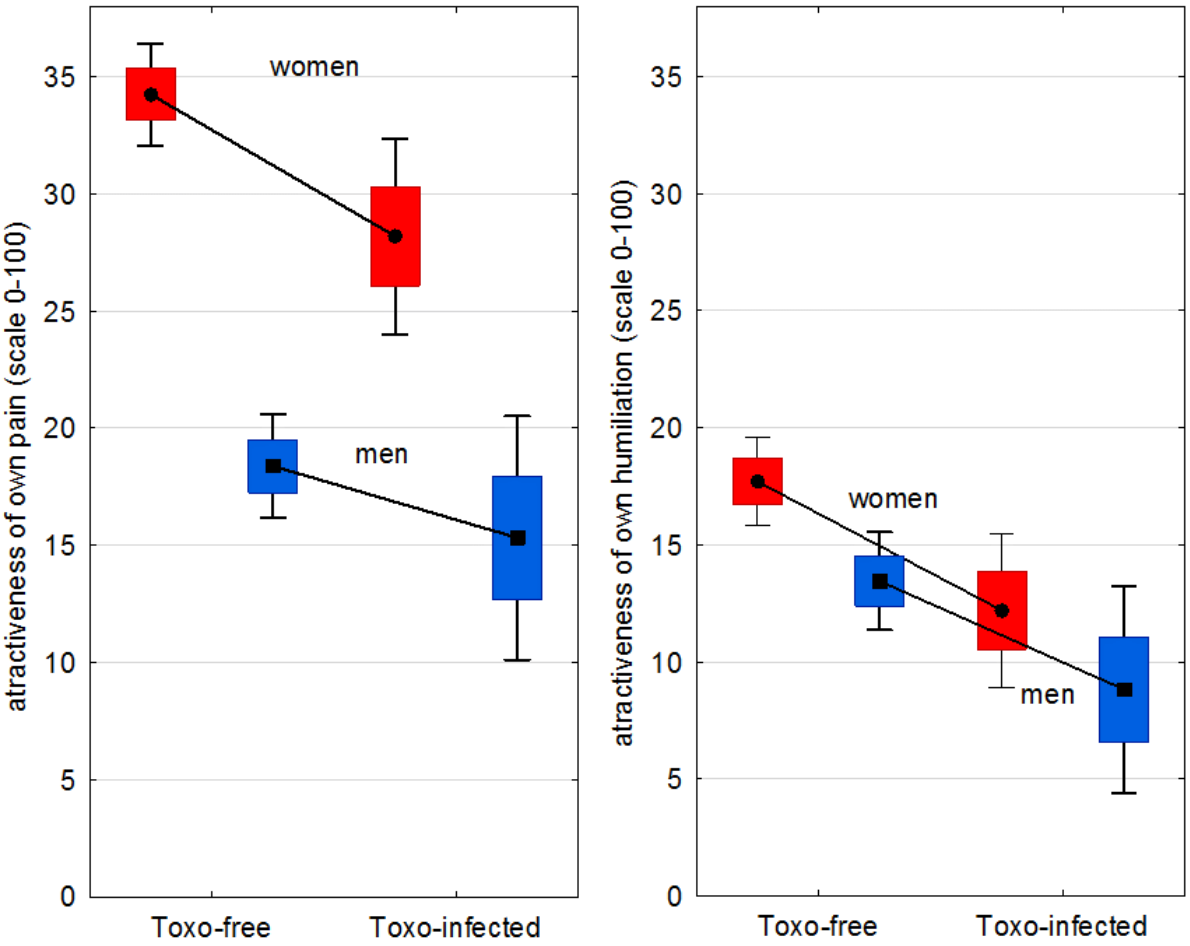
The close connection between fear and sexual arousal also exists in humans. The fraction of subjects who are sexually aroused by fear, pain and humiliation, or who are even involved in sadomasochistic sexual practices is rather high [8] and it is often suggested that sadomasochistic preferences and activities could increase biological fitness of individuals. [9] However, the existence of sadomasochism could also be just a side-effect of capacity of co-activation of fear- and sex-related circuits in the amygdala. If this is true, then the sadomasochistic preference could occur in higher frequencies in *Toxoplasma*-infected subjects. To test this hypothesis, we searched for a positive association between sadism- and masochism-related preferences among the population of 36,564 subjects (5,087 *Toxoplasma*-free and 741 *Toxoplasma*-infected) using a Facebook-based snowball method.[10] The question regarding subjects' toxoplasmosis status of subjects was mixed among 700 other questions, and the subjects were not informed that the study concerned the effects of toxoplasmosis. Factor analyses showed that 24 independent factors explained 53 % of variability in sexual behavior of the participants. After the correction for multiple tests, 7 and 10 of these 24 factors correlated with toxoplasmosis in women and men, respectively. The factor *Arousal by violence* correlated positively with toxoplasmosis in women ($p=0.014$), and factors *Arousal by submission and masochism* ($p=0.004$), *Arousal by raping* ($p=0.001$), and *Arousal by sexual*

bondage ($p<0.0005$) correlated positively with toxoplasmosis in men. Both women and men were less aroused by *Sexual dominance and sadism* and both practiced any kind of sadomasochistic sex less often than their *Toxoplasma*-free peers (all $p<0.0005$). Other factors correlated with toxoplasmosis, e.g. zoophilia and homosexual sex (not the homosexual orientation), had no direct relation to BDSM or fear. [10] Generally, infected subjects expressed relatively high attraction to nonconventional sexual practices, especially certain BDSM-related practices, but they also reported to perform such activities less often than the *Toxoplasma*-free subjects.

The *Toxoplasma* infection seems to have an opposite effect on the human sexual preference and on the sexual behavior. Therefore, it is difficult to detect these effects using simple univariate statistical techniques, for example, by studying the effect of the infection on sexual preference, without controlling for the effect of the infection on sexual activity and sexual desire. For example, *Toxoplasma*-infected subjects scored higher than their *Toxoplasma*-free peers in the factor *Arousal by submission and masochism* when the other sex-related variables were controlled in the process of factor analysis.[10] However, they scored lower when asked how much they are aroused by being humiliated, or by suffering pain, two traits that positively load the factor *Arousal by submission and masochism* see the Figure 1. *Toxoplasma* is known to affect many physiological variables which can independently, directly or indirectly, affect various behavioral traits in humans and rodents. For example, *Toxoplasma* transiently increases the concentration of testosterone,[11] which could increase sexual desire and sexual activity in men during the first years after the infection. However, it also has a strong impact on the immunity and health of infected individuals.[12,13] There is strong indirect evidence that the infected subjects suffer a mild but long term chronic stress. All these factors have negative impacts on sexual desire and sexual activity of infected hosts.

Some of the *Toxoplasma*-related effects are more specific. *Toxoplasma* codes two genes for tyrosine hydroxylases, the rate limiting enzymes for the synthesis of dopamine.[14] A large amount of this transmitter has been detected within and nearby pseudocysts of *Toxoplasma* in the brain tissue of infected hosts.[15] This increased concentration of dopamine could explain the approximately 2.7 times higher risk of schizophrenia in *Toxoplasma*-infected subjects,[16,17] as well as more serious course of schizophrenic illness in *Toxoplasma*-infected patients.[18] A high concentration of dopamine is also known to have a negative effect on the personality factor novelty seeking[19] and a decrease of this factor has indeed been observed in *Toxoplasma*-infected humans[20,21] as well as in rodents infected by *Toxoplasma* in laboratory studies.[22,23] The lower factor novelty seeking will, probably, result in a lower affinity toward non-conventional sexual practices and techniques among *Toxoplasma*-infected subjects. Another neurophysiological effect of toxoplasmosis is a decrease of the concentration of tryptophan and therefore also serotonin, and an increase of some of their metabolites, namely the kyneuric acids.[24] Tryptophan is the aminoacid that is essential for growth of many microorganisms and its depletion is an important part of a nonspecific protective reaction of the host organism against bacterial and protozoan infections.[25] The shifts in concentration of these molecules, especially the decrease of serotonin, could explain the observed higher incidence of attempted suicides in the *Toxoplasma*-infected subjects; however, it can also negatively affect their sexual desire and activity. The last *Toxoplasma*-associated effect is the hypomethylation of regulatory elements of some genes, e.g. arginine vasopressin promoter, in medial amygdala, resulting in co-activation of sex-related circuits by fear-related stimuli.[4] This could result not only in the FAP but also in the increase of masochistic preferences in *Toxoplasma*-infected subjects.

Figure 1 Differences in the attraction to self-pain and humiliation between *Toxoplasma*-infected and *Toxoplasma*-free subjects.



When we study a particular effect of toxoplasmosis (or of any other biotic, abiotic or social factor) on the organisms' behavior (or any other multifaceted dependent variable), we have to disentangle a complex networks of forces influencing the focal variable. We must always take into an account that when we, for example, measure masochistic preferences using a questionnaire, the obtained data reflect not only these preferences, but also sexual desire, novelty seeking, neuroticism, pretension and several other personality traits. Some of these traits could be also influenced by the factor under the study, e.g. the *Toxoplasma* infection, and some of them could have a stronger and sometimes an opposite effect on the dependent variable than the focal factor. The only way to solve this principal problem is to abandon

simple univariate methods of analyzing the statistical associations in favor of more complex multivariate statistical techniques. For this task, however, we need much larger data sets – preferably thousands of subjects – than the data sets that are sufficient for univariate analyses. We must also be prepared to accept the fact that observed effects usually explain only a small part of the total variability of the dependent variable and that the results of proper more complex analysis could seemingly contradict the results of simple univariate analyses.

Acknowledgement

I would like to thank Charlie Lotterman for his help with the final version of the paper. The work was supported by project UNCE 204004 (Charles University in Prague) and the Czech Science Foundation (Grant No. P407/16/20958).

References

1. Flegr J. Influence of latent toxoplasmosis on the phenotype of intermediate hosts. Folia Parasitol 2010; 57:81-7.
2. Berdoy M, Webster JP, Macdonald DW. Fatal attraction in rats infected with *Toxoplasma gondii*. Proc R Soc Biol Sci Ser B 2000; 267:1591-4.
3. Flegr J, Lenochová P, Hodný Z, Vondrová M. Fatal attraction phenomenon in humans: cat odour attractiveness increased for *Toxoplasma*-infected men while decreased for infected women. PLoS Neglect Trop D 2011; 5:e1389.
4. Dass SAH, Vyas A. *Toxoplasma gondii* infection reduces predator aversion in rats through epigenetic modulation in the host medial amygdala. Mol Ecol 2014; 23:6114-22.
5. Flegr J, Markos A. Masterpiece of epigenetic engineering - how *Toxoplasma gondii* reprogrammes host brains to change fear to sexual attraction. Mol Ecol 2014; 23:5934-6.

6. Poirotte C, Kappeler PM, Ngoubangoye B, Bourgeois S, Moussodji M, Charpentier MJE. Morbid attraction to leopard urine in *Toxoplasma*-infected chimpanzees. Cur Biol 2016; 26:R98-R99.

7. 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 Nat Acad Sci USA 2007; 104:6442-6447.

8. Jozífkova E, Bartoš L, Flegr J. Evolutional background of dominance/submissivity in sex and bondage: the two strategies? Neuroendocrinol Lett 2012; 33: 636-642.

9. Jozífková E, Flegr J. Dominance, submissivity (and homosexuality) in general population. Testing of evolutionary hypothesis of sadomasochism by internet-trap-method. Neuroendocrinol Lett 2006; 27:711-718.

10. Flegr J, Kuba R. The relation of *Toxoplasma* infection and sexual attraction to fear, danger, pain and submissiveness. Evol Psych 2016:1-10.

11. Flegr J, Lindová J, Pivoňková V, Havlíček J. Brief Communication: Latent toxoplasmosis and salivary testosterone concentration-important confounding factors in second to fourth digit ratio studies. Am J Phys Anthropol 2008; 137:479-84.

12. Flegr J, Stříž I. Potential immunomodulatory effects of latent toxoplasmosis in humans. BMC Infect Dis 2011; 11:274.

13. Flegr J, Escudero DQ. Impaired health status and increased incidence of diseases in *Toxoplasma*-seropositive subjects – An explorative cross-sectional study. Parasitology 2016; 143:1974-89.

14. Gaskell EA, Smith JE, Pinney JW, Westhead DR, McConkey GA. A unique dual activity amino acid hydroxylase in *Toxoplasma gondii* PLoS ONE 2009; 4:e4801.

15. Prandovszky E, Gaskell E, Martin H, Dubey JP, Webster JP, McConkey GA. The neurotropic parasite *Toxoplasma gondii* increases dopamine metabolism. PLoS ONE 2011; 6:e23866.
16. Torrey EF, Bartko JJ, Lun ZR, Yolken RH. Antibodies to *Toxoplasma gondii* in patients with schizophrenia: A meta-analysis. Schizophr Bull 2007; 33:729-36.
17. Torrey EF, Bartko JJ, Yolken RH. *Toxoplasma gondii* and other risk factors for schizophrenia: An update. Schizophr Bull 2012; 38:642-7.
18. Holub D, Flegr J, Dragomirecka E, Rodriguez M, Preiss M, Novak T, et al. Differences in onset of disease and severity of psychopathology between toxoplasmosis-related and toxoplasmosis-unrelated schizophrenia. Acta Psychiatr Scand 2013; 127:227-38.
19. Cloninger CR, Svrakic DM, Przybeck TR. A psychobiological model of temperament and character. Arch Gen Psychiatry 1993; 50:975-90.
20. Flegr J, Preiss M, Klose J, Havlíček J, Vitáková M, Kodym P. Decreased level of psychobiological factor novelty seeking and lower intelligence in men latently infected with the protozoan parasite *Toxoplasma gondii*. Dopamine, a missing link between schizophrenia and toxoplasmosis? Biol Psychol 2003; 63:253-68.
21. Skallová A, Novotná M, Kolbeková P, Gašová Z, Veselý V, Flegr J. Decreased level of novelty seeking in blood donors infected with *Toxoplasma*. Neuroendocrinol Lett 2005; 26:480-6.
22. Skallová A, Kodym P, Frynta D, Flegr J. The role of dopamine in *Toxoplasma*-induced behavioural alterations in mice: an ethological and ethopharmacological study. Parasitology 2006; 133:525-35.
23. Hodková H, Kodym P, Flegr J. Poorer results of mice with latent toxoplasmosis in learning tests: impaired learning processes or the novelty discrimination mechanism? Parasitology 2007; 134:1329-37.

24. Silva NM, Rodrigues CV, Santoro MM, Reis LFL, Alvarez-Leite JI, Gazzinelli RT. Expression of indoleamine 2,3-dioxygenase, tryptophan degradation, and kynurenine formation during in vivo infection with *Toxoplasma gondii*: Induction by endogenous gamma interferon and requirement of interferon regulatory factor 1. Infect Immun 2002; 70:859-68.
25. MacKenzie CR, Heseler K, Muller A, Daubener W. Role of indoleamine 2,3-dioxygenase in antimicrobial defence and immuno-regulation: Tryptophan depletion versus production of toxic kynurenines. Curr Drug Metab 2007; 8:237-44.