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SHORT COMMUNICATION

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

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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 in mice, or smell of leopards in chimpanzees, start to additionally co-activate sexual arousal-related circuits in the infected animals. 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.

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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 4 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 biologic 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 toxoplasmosis status of subjects was mixed among 700 other questions, and the subjects were not informed that the study concerned the

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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, 2 traits that positively load the factor *Arousal by submission and masochism* see the Fig. 1.

Toxoplasma is known to affect many physiologic 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 2 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.

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, protension 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

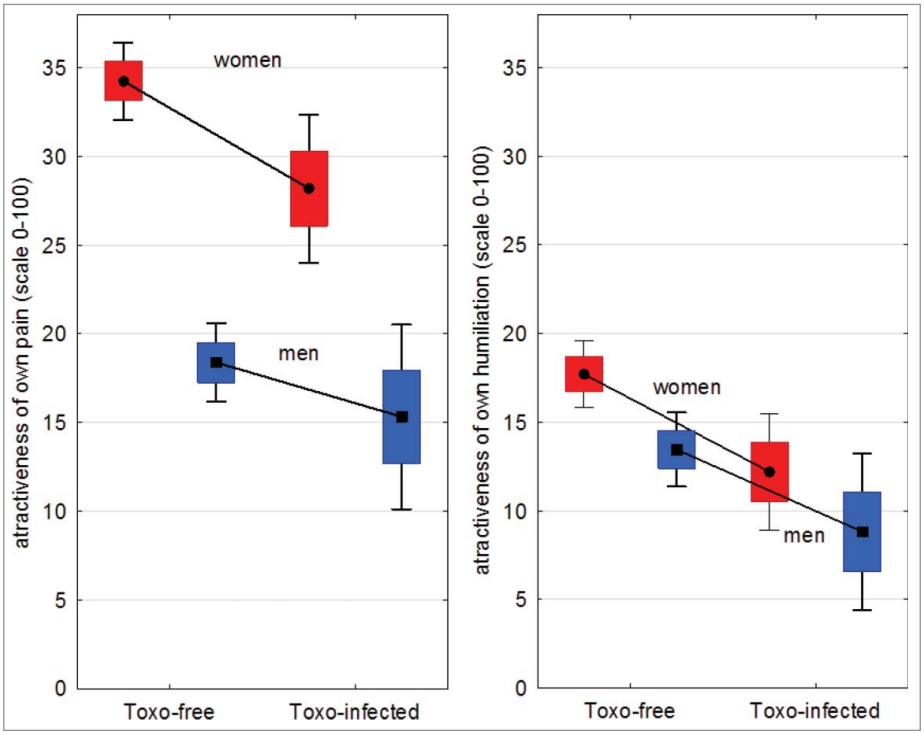

Figure 1. Differences in the attraction to self-pain and humiliation between *Toxoplasma*-infected and *Toxoplasma*-free subjects.

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.

Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

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