

EDITORIAL INTRODUCTION

Influence of latent toxoplasmosis on the phenotype of intermediate hosts

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The influence of latent toxoplasmosis on the phenotype, especially on the behaviour, of intermediate hosts has been intensively studied since the mid-1990s. The number of papers dealing with this topic that can be found in the Web of KnowledgeSM by using the combination of terms *toxoplasm* AND (behavi* OR psychol* OR personalit* OR psychiatri* OR schizophr*)* is rapidly increasing from only 3 papers in 1990–1994 (all published in 1994) and 4 papers in 1995–1999 to 25 papers in 2000–2004 and 45 papers in 2005–2009. However, this boom was preceded by more than 10 papers of British authors around Hutchinson, Hay, Aitken and Arnott in the 1980s. Most of these papers studied the influence of congenital or acute toxoplasmosis on the behaviour of laboratory infected mice; however, some of them also focused on the behavioural impacts of latent (or chronic in their terminology) toxoplasmosis. Even earlier, sporadic works suggested a relation between latent or acute toxoplasmosis and some psychiatric disorders, in particular schizophrenia. The comprehensive review from 2007 (Torrey et al. 2007) lists 11 studies published in 1957–1980; however, several other studies, mostly case reports, that appeared in the 1940s and 1950s showed or suggested that acute toxoplasmosis was relatively often associated with pronounced psychiatric symptoms (Jírovec and Vojtěchovský 1957).

The sharply increasing interest in the influence of latent toxoplasmosis on the host phenotype in the past two decades has both objective and subjective causes.

The major objective cause is that about one third of the world population have been infected with *Toxoplasma gondii* and latent toxoplasmosis that was until recently considered as asymptomatic has been shown to have the potential to have serious consequences for physical and psychical health. The strongest association was found between toxoplasmosis and schizophrenia, suggesting that toxoplasmosis might trigger this devastating psychiatric disorder in predisposed subjects or modulate the course of the disease. Latent toxoplasmosis seems to increase the risk of suicide (Arling et al. 2009) and four independent studies also found increased risk of traffic accidents in *Toxoplasma gondii*-infected subjects (Flegr et al. 2002, 2009, Yerehi et al. 2006, Ko-

cazeybek et al. 2009). Consequently, latent toxoplasmosis might be indirectly responsible for about one million deaths in traffic accidents, about as many deaths might result from increased risk of occupational injuries and possibly hundreds of thousands of deaths might be due to increased risk of suicide. Latent toxoplasmosis has a strong effect on reproduction in animal hosts of the parasite, including humans. It negatively influences the rate of development of early embryos (Flegr et al. 2005a, Kaňková and Flegr 2007) and shifts the sex ratio towards males in the early phase of *Toxoplasma* infection and towards females in the later phases (Kaňková et al. 2007a). The results of an earlier study showing that mothers of children with Down syndrome had an 84% prevalence of toxoplasmosis (while its rates in fathers as well as in the general population were about 30%) (Hostomská et al. 1957) suggest that *T. gondii* might suppress some forms of cellular immunity and by doing so might increase the chance for survival of more immunogenic male embryos or embryos with developmental defects. Anecdotal observations on a group of 15 infected mice provide a possible explanation for the reported higher proportion of daughters in women and female offspring in mice with very old infection. The mice infected for more than 18 months manifested several symptoms of deteriorated health such as extensive hair loss, paralysis or blindness (Fig. 1). The controls that showed no such symptoms, remained in good physical condition for more than 30 months. Therefore, the Trivers-Willard effect, i.e. a higher proportion of the female offspring in the females in poor physical condition, is likely to be responsible for the decreased sex ratio in women and mice with very old *Toxoplasma* infection. Severe impairment of health in infected mice (which did not differ from controls 2–4 months after the infection) could also provide an (alarming) explanation for the decreased seroprevalence of toxoplasmosis in the highest age strata reported in human studies, i.e. the premature death of the infected subjects.

Another objective reason for the increased interest in the influence of latent toxoplasmosis on the host phenotype is that the observed phenomena are a challenge

for basic research. *Toxoplasma gondii* is one of many parasites that manipulate the phenotype, in particular the behaviour, of their hosts to increase the chance of their transmission from intermediate to definitive host by predation. However, *T. gondii* is a very common parasite that frequently infects even humans in both developing and developed countries. It has spectacular effects on the behaviour of mice and rats; in particular it is able to convert the innate fear that rodents have of cat odours into an attraction to them (Berdyozov et al. 2000). The behavioural changes induced by *T. gondii* in humans are less conspicuous. They explain, as a rule, a few percentages of variation in a particular behavioural trait; however, since they affect the human species, they attract the attention not only of scientists but also of the general public. People with latent toxoplasmosis exhibit characteristic shifts in the personality profile and behaviour (Flegr 2007) as observed in ethological experiments (Lindová et al. 2006). The shifts usually increase with the duration of *Toxoplasma* infection which implies that toxoplasmosis induces the observed behavioural shifts rather than that the subjects with a particular personality type and behaviour are at a higher risk of *Toxoplasma* infection (Flegr et al. 2000). Results of a correlation study suggest that the differences in the prevalence of toxoplasmosis between countries could explain a significant part of the variance in aggregate neuroticism among populations (Lafferty 2005, 2006).

Toxoplasmosis also influences the morphology of infected persons. Infected men are higher, have a lower second to fourth digit length ratio in the left hand (Flegr et al. 2005b, 2008a), i.e. have longer fingers (Kratochvíl and Flegr 2009), and their faces in photographs are rated by female raters as more dominant (Hodková et al. 2007b). All these traits can be related to the higher concentration of testosterone observed in *T. gondii*-infected men (while in infected women, the concentration of testosterone was decreased) (Flegr et al. 2008b).

Four recent studies have shown that the influence of toxoplasmosis depends on RhD phenotype. Toxoplasmosis has a strong effect on RhD-negative subjects, while RhD-positive homozygotes are influenced much less and RhD-positive heterozygotes seem to resist the toxoplasmosis-induced changes. RhD phenotype has been shown to influence the responses of the body to latent toxoplasmosis in several respects: changes in reaction times (Flegr et al. 2008c, Novotná et al. 2008), risk of traffic accidents (Flegr et al. 2009), psychological profile (Flegr et al. 2010) and maternal weight gain during pregnancy (Kaňková et al. 2010). The superiority of RhD-positive heterozygotes could provide the key to the about 60-year-old enigma of sustaining the stable RhD polymorphism in the human population as well as to the striking differences in the frequency of RhD-negativity among populations – that might result from the equally striking differences in the *T. gondii* prevalence rates (Flegr et al. 2008c).

Probably the most interesting recent findings in *Toxoplasma* research is the discovery of two genes for tyrosine hydroxylases in the *T. gondii* genome (Gaskell et al. 2009). These enzymes catalyse the rate-limiting step in the synthesis of dopamine in the brain tissue and their expression in *T. gondii* tissue cysts in the host's brain can explain a variety of psychological and psychiatric symptoms observed in subjects with acute or latent toxoplasmosis as well as many ethological changes in infected animals. It is important to remind here that a disturbance in the concentration of dopamine in certain parts of the brain is considered to play an important role in the development of schizophrenia and that an increased dopamine concentration influences the ability to recognize novelty in mammals, including humans.

There are at least three subjective reasons for the increased interest in the behavioural effects of latent toxoplasmosis. The most important reason is the publication of a seminal paper of Torrey and Yolken with their hypothesis about the aetiological role of *Toxoplasma* infection in schizophrenia disease (Torrey and Yolken 1995) and the following broad activities of the Stanley Research Institute (formerly the Stanley Foundation), including the organisation of two international meetings and funding of many interesting research projects. The second reason was the publication of several interesting and widely cited discoveries concerning the behavioural changes in *T. gondii*-infected rats by the Oxford group of Joanne P. Webster (Berdyozov et al. 1995a, b, Webster et al. 1994, Webster 1994). The third reason was the start of research activities of the Prague team of parasitologists that systematically studies the influence of latent toxoplasmosis on the human behaviour.

I can only speculate what triggered the studies of other research teams, but the studies of the Prague group started thanks to a happy coincidence and to the Velvet Revolution. Returning from my one-year stay at the Department of Immunology of the University of Tokyo in 1991, I was allowed to leave my “exile” at the Institute of Molecular Genetics of the Academy of Science for the Faculty of Science, Charles University. I came back to the Department of Parasitology and to the lab of Professors Čerkasov and Kulda where I had finished my PhD studies five years earlier. There, a long tradition of *Toxoplasma* research existed since the time of the founder of Czech parasitology, Professor Otto Jirovec. Among other things, an antigen for diagnostic kits was developed, produced and tested (and later only tested) there. As a result, I learned that I was among the privileged *T. gondii*-infected subjects. (I had the privilege of being a guinea pig to my colleagues who kept trying to inject me with the *Toxoplasma* antigen while testing every new batch of it. Fortunately, I was unaware then that the skin test might trigger not only the local immune response but also psychiatric symptoms in a certain proportion of subjects [Jirovec and Vojtěchovský 1957].) At that time I was reading (and not



Fig. 1. *Toxoplasma gondii*-infected mouse 18 months after laboratory infection. Note the skin lesions and absence of the right eye. Female F1 crosses between mouse inbred strains BALB/c (females) and C57 BL (males) (AnLab, Czech Republic) infected at an age of 10 weeks with avirulent HIF strain of *Toxoplasma gondii* (Hodková et al. 2007a) were group-housed in plastic cages, 7–8 animals per cage, with wood shaving bedding and maintained on a 12-h light/dark cycle (dark from 2 p.m.) for 20 months. No difference was observed in the appearance and weight between infected and control mice 7 weeks after the infection.

for the first time) *The Selfish Gene* by Richard Dawkins (Dawkins 1976). It may have been this book that inspired me to think about a possible role of the parasite present in my brain, the parasite that is inclined to move from my tissue to the stomach of a feline predator, in some surprising patterns in my behaviour. I was long puzzled why I was gladly and actively searching for trouble, why I remained cool while in imminent danger (e.g. under machine gun fire in eastern Turkey) and why, on the other hand, I was giving up prematurely the physical fight. In the early postcommunist era, even young scientists could freely choose their topic of research. Therefore, I decided to test my hypothesis about the possible influence of latent toxoplasmosis on the human personality. Given the lack of funds for research at that time, I chose the cheapest possible method, a questionnaire survey. Using the introspection method, I produced a list of ten questions (or rather question areas) expected to be answered differently before and after the infection (see legend of Table 1). As some of them were somewhat curious, they were added to follow after 186 questions of Cattell's 16 personality factor questionnaire that was then widely used in clinical practice in the Czech Republic. Subsequently, I invited my colleagues, biology faculty and students to test a new batch of the *Toxoplasma* antigen and asked them to fill in the modified Cattell's questionnaire. After about two years, data from nearly three hundred subjects were available, with approximately 25% of the respondents being *Toxoplasma*-infected, and I could compare the answers from *Toxoplasma*-free and *Toxoplasma*-infected subjects.

I made two unexpected discoveries. One was rather displeasing – I found no difference in the responses to

my ten questions between *Toxoplasma*-free and *Toxoplasma*-infected subjects, while the other was pleasing – *Toxoplasma*-free and *Toxoplasma*-infected subjects differed in some personality factors measured with Cattell's personality questionnaire, initially only used to draw away the attention of the respondent from my own "Toxo-questions" (Flegr and Hrdý 1994). And I was captured! In the following 15 years we reproduced the original results on independent sets of students, blood donors, soldiers and confirmed them by using other personality questionnaires and ethological tests. We studied the problems of causality and physiological mechanisms of the observed changes. Later on, we also focused on the influence of latent toxoplasmosis on human morphology and reproduction biology. About 3 years ago, I happened to go through the results of the original Toxo-questionnaire. And again I was surprised. When more proper nonparametric statistical technique was used for the analysis of the original data, namely the partial Kendall regression that enables to control for the influence of confounding covariates (Kaňková et al. 2010), here the age, some differences in the responses of *Toxoplasma*-free and *Toxoplasma*-infected subjects were, in fact, pretty significant. As we continued to use more or less automatically our modified Cattell's questionnaire in the following studies, we were able to verify our surprising results in other independent experimental sets (see Table 1). We can only speculate if the responses of *Toxoplasma*-infected probands are objectively true or only reflect the subjective feelings. However, at least some subjective statements of *Toxoplasma*-infected subjects, e.g. about their unnaturally slow reaction while in imminent danger, can be easily experimentally tested.

This special issue of *Folia Parasitologica* features three review articles and six research papers. Ajai Vyas and Robert Sapolsky (Vyas and Sapolsky 2010) present the state-of-the-art knowledge on the molecular and neurophysiological mechanisms of the behavioural effects of latent toxoplasmosis. They focus mainly on the fatal attraction phenomenon, i.e. the ability of *T. gondii* to convert the innate fear that rodents have of cat odours into an attraction to them, and discuss possible proximate mechanisms that might be involved in it. They suggest, among other things, that the preferential location of the *T. gondii* tissue cysts in the amygdala, the part of the brain that is involved in the normal fear response, and the expression of two genes for the enzymes that catalyze the rate-limiting step in the synthesis of dopamine in *T. gondii*, may provide the hints for the nature of the proximal mechanisms in play.

The article of Joanne P. Webster and Glenn A. McConkey (Webster and McConkey 2010) is a related but rather complementary review. The authors summarize all known behavioural effects of latent toxoplasmosis and discuss possible proximal mechanisms that can be responsible for these effects. They show that dopamine and tryptophan metabolites in general seem to be suspicious players in the field. They also analyze the well-known relationship between toxoplasmosis and schizophrenia and consider, with caution, the assumption that the therapeutic effects of some antipsychotic drugs might be in fact mediated by the inhibition of the proliferation of parasites (but compare Fekadu et al. 2010).

The third review of Abebaw Fekadu, Teshome Shibre and Anthony J. Cleare (Fekadu et al. 2010) provides a comprehensive overview of the literature about the relationship between *Toxoplasma* infection and behavioural disorders in humans. It pays attention not only to the relationship between toxoplasmosis and schizophrenia but also affective disorder, obsessive-compulsive disorder and personality and behavioural changes observed in the normal population. The role of toxoplasmosis in the aetiology of psychiatric morbidity and possibly involved mechanisms as well as results of some still-unpublished intervention studies are discussed.

The paper of William H. James (James 2010) presents and thoroughly discusses his hypothesis suggesting that many parasites and pathogens change the concentration of steroid hormones, here testosterone and oestrogen, of infected hosts which often results in a shift in the sex ratio, the proportion of males in the offspring. He provides indirect evidence that this is the case during the infection with hepatitis B and C viruses and direct evidence that the shift occurs during latent infection with *T. gondii*. An alternative hypothesis explaining the *Toxoplasma*-associated sex ratio shift suggests that the phenomenon is caused by a higher probability of survival of more immunogenic male embryos due to *T. gondii*-induced immunosuppression (Kaňková et al. 2007a, b) seems to be

able to explain a broader spectrum of related phenomena, including the higher proportion of children with Down syndrome in *Toxoplasma*-infected subjects (Hostomská et al. 1957). However, it should be reminded that the proximate mechanism of immunosuppression remains unknown and might involve the parasite-induced shift in steroid hormones.

The paper of Pelin Yuksel et al. (Yuksel et al. 2010) presents the surprising results of the analysis of a large sample of schizophrenic patients (300 patients and 300 controls). The authors speculate that another still unidentified pathogen also transmitted by cat rather than *T. gondii* might play a role in the well-known association between toxoplasmosis and schizophrenia in Turkey, since this strong association disappeared when the contact with a cat was included into the model as an independent variable. The results even suggest that the subjects reporting no contact with a cat were protected by toxoplasmosis against schizophrenia. Nevertheless, the challenging assumption that toxoplasmosis may only be an indirect indicator of the previous contact with a cat (and with the still unidentified pathogen) needs to be confirmed by further independent studies.

Actually, an independent support for the hypothesis of an unknown aetiological agent transmitted by the cat is provided in the article of Dunja Hinze-Selch et al. (Hinze-Selch et al. 2010). They report a strong association between latent *Toxoplasma* infection and subsequently diagnosed personality disorder observed in a large population of patients with schizophrenia. Surprisingly, they also find the negative (but here nonsignificant) association between toxoplasmosis and schizophrenia when the contact with a cat was controlled.

The results presented by Jitka Lindová and coworkers (Lindová et al. 2010) provide new evidence for the latent toxoplasmosis-induced shift in human behaviour. The experimental game method was used to compare the behaviour of *Toxoplasma*-infected and *Toxoplasma*-free subjects and the obtained results were consistent with the data collected earlier using psychological questionnaires and ethological experiments. The difference in the behavioural response to *Toxoplasma* infection between the infected men and women is explained by psychological mechanisms, namely the opposite reactions of men and women to chronic stress. In this context, latent toxoplasmosis might be considered as an important but still neglected long-term stressor. Of course, the exposure to chronic stress in people with latent toxoplasmosis should be confirmed by independent (and preferably more direct) methods.

The results of Jaroslav Flegr et al. (Flegr et al. 2010) suggest that the Rh blood group might modify psychological responses of humans to the effects of latent toxoplasmosis as can be seen from the personality profile measured with Cattell's 16PF questionnaire and Cloninger's TCI

Table 1. Differences between responses of *Toxoplasma*-infected and *Toxoplasma*-free subjects to 10 questions of the “Toxo-questionnaire” constructed by the introspection method in 1992 to test the hypothesis that the author’s behaviour is manipulated by *Toxoplasma gondii*. In 2000–2007, the question “Reflexes” was only included into Cattell’s 16PF test. In 2000–2004, the difference between *Toxoplasma*-infected and *Toxoplasma*-free students was also significant (Tau=0.154, p=0.048). The students tested in 2005–2007 and blood donors tested in 1999–2001 showed nonsignificant differences depending on *Toxoplasma* status. Before 2007, modified Cattell’s questionnaire was administered in hard copy form. The students tested in 2007–2009 were administered the questionnaire in electronic form and a 5-step instead of 3-step Licker-type scale was used to express agreement/disagreement with the positively formulated responses to particular questions or rather question areas (see below). The partial Kendall regression with the age as a covariate (Kaňková et al. 2010) was used to test the strength and significance of association of latent toxoplasmosis and the responses. Results of the more conservative two-sided test were always listed despite the fact that the direction of the effect for all questions agreed with the *a priori* hypotheses and therefore more sensitive one-tailed tests should have been used. The results significant in one-tailed tests are printed in bold. The second column shows the number of subjects (total, *Toxoplasma*-infected/*Toxoplasma*-free). The first and second sets are related; the set Faculty includes not only the biology faculty members but also set 2 students. List of question areas: **Diplomacy:** Diplomacy is not my strong point; I am not very good at dealing with others. I often fail diplomacy by managing to offend the person I need to win. If I have a bad opinion about somebody and I do not want him/her to know, I usually fail to hide it. When trying to compliment somebody, I often offend him/her. **Conflicts:** An unexpected encounter with a shameless, rude or bad person usually takes me by surprise, in such situations I am not able to defend myself effectively. When I have to pay a craftsman for his work, I usually do so even if he has failed to do the work properly. When a shop assistant is trying to cheat me, I usually put up with it. **Reflexes:** My instinctive (reflex) behaviour under imminent danger is rather slow and passive. In a situation where most people get alarmed and instinctively jump aside, I am slow to react. When a car horn honks at me, I tend to do nothing, although in danger, and to let it to run over rather than to run under the wheels of another car. **Hypnosis:** I believe that some people have the power to impose their will on others under hypnosis or otherwise. **Hypnotised:** I suspect that I have already succumbed to a hypnotic suggestion, at least once. **Defence:** I remember a situation where I realized I was doing or saying something that is against my own interests, against the logic, something that I would not expect from myself or from any other person in the same situation. Instead of stopping doing so and starting to behave normally, I continued the initial action with an intense feeling of inappropriateness and astonishment about what I was doing. **Troubles:** I can appear to people in my surroundings to be someone who is always calling for trouble and engaging in needless conflicts. I never hesitate to stir up a hornet’s nest. **Surrender:** When I am attacked, physically or otherwise, or when I should fight for something important, I stop fighting at a moment. It is not a result of a rational decision not to fight, as in fact I know that I should continue fighting and I would like to do so, but my own subconsciousness betrays me and I lose the will to fight back. **Zoophobia:** I have strong unpleasant feelings when I take a close look at a snake or a big spider. (Here, the negative answer of a *Toxoplasma*-infected subject was expected.) **Self-preservation:** I have a weak instinct for self-preservation: in situations where somebody else might be afraid, for example being alone in forest at night or in an empty house, I remain cool.

| Set | | | Diplomacy | Conflicts | Reflexes | Hypnosis | Hypnotised | Defence | Troubles | Surrender | Zoophobia | Self-pres- ervation |
|------------------------|---------------------|-----|--------------|--------------|--------------|--------------|--------------|---------|--------------|--------------|-----------|------------------------|
| Faculties 1992–1995 | All (443, 113/330) | Tau | 0.066 | 0.053 | 0.106 | 0.112 | 0.018 | 0.018 | 0.046 | 0.047 | -0.004 | 0.023 |
| | | p | 0.037 | 0.095 | 0.001 | 0.000 | 0.561 | 0.579 | 0.151 | 0.143 | 0.905 | 0.460 |
| | Men (243, 69/174) | Tau | 0.108 | 0.062 | 0.189 | 0.134 | 0.025 | 0.050 | 0.070 | 0.143 | 0.052 | 0.053 |
| | | p | 0.012 | 0.151 | 0.000 | 0.002 | 0.567 | 0.245 | 0.104 | 0.001 | 0.228 | 0.218 |
| | Women (200, 44/156) | Tau | -0.027 | 0.020 | 0.045 | -0.028 | 0.085 | 0.023 | -0.026 | 0.000 | -0.058 | -0.104 |
| | | p | 0.574 | 0.678 | 0.342 | 0.562 | 0.073 | 0.632 | 0.583 | 0.995 | 0.226 | 0.029 |
| Students 1992–1995 | All (310, 68/242) | Tau | 0.046 | 0.057 | 0.094 | 0.123 | 0.027 | -0.053 | 0.056 | 0.039 | 0.010 | 0.021 |
| | | p | 0.232 | 0.136 | 0.013 | 0.001 | 0.471 | 0.167 | 0.143 | 0.304 | 0.791 | 0.577 |
| | Men (162, 42/120) | Tau | 0.121 | 0.069 | 0.163 | 0.141 | 0.024 | -0.048 | 0.058 | 0.156 | -0.003 | 0.009 |
| | | p | 0.023 | 0.194 | 0.002 | 0.008 | 0.644 | 0.366 | 0.274 | 0.003 | 0.949 | 0.860 |
| | Women (148, 26/122) | Tau | -0.029 | 0.060 | -0.002 | 0.124 | 0.069 | -0.041 | 0.046 | -0.061 | -0.032 | -0.043 |
| | | p | 0.604 | 0.281 | 0.967 | 0.025 | 0.214 | 0.459 | 0.408 | 0.269 | 0.564 | 0.439 |
| Mothers 1997 | 191, 55/136 | Tau | 0.116 | 0.012 | 0.095 | 0.010 | 0.006 | 0.049 | 0.132 | 0.026 | 0.044 | -0.045 |
| | | p | 0.017 | 0.813 | 0.051 | 0.843 | 0.900 | 0.315 | 0.007 | 0.596 | 0.370 | 0.354 |
| Students 2007–2009 | All (323, 276/47) | Tau | 0.018 | -0.042 | -0.007 | -0.027 | -0.001 | nd | nd | 0.062 | 0.001 | 0.017 |
| | | p | 0.627 | 0.262 | 0.859 | 0.467 | 0.976 | nd | nd | 0.098 | 0.978 | 0.643 |
| | Men (109, 92/17) | Tau | -0.101 | -0.022 | 0.011 | 0.148 | 0.001 | nd | nd | 0.123 | -0.060 | -0.012 |
| | | p | 0.120 | 0.732 | 0.871 | 0.022 | 0.992 | nd | nd | 0.058 | 0.358 | 0.858 |
| | Women (214, 184/30) | Tau | 0.077 | -0.057 | -0.018 | -0.116 | -0.001 | nd | nd | 0.020 | 0.030 | 0.033 |
| | | p | 0.093 | 0.212 | 0.698 | 0.012 | 0.979 | nd | nd | 0.662 | 0.514 | 0.470 |

questionnaire. In addition to the already known effects of toxoplasmosis on novelty seeking, self-transcendence, superego strength and protension, the new study has found effects of the RhD phenotype on ego strength, protension, and praxernia as well as opposite effects of toxoplasmosis on ego strength, praxernia, ergic tension and cooperativeness in Rh-positive and Rh-negative subjects.

Geetha Kannan et al. studied the behavioural effects of *Toxoplasma* infection on laboratory mice (Kannan et al. 2010). They used two different strains of *T. gondii* and repeated the tests two and seven months after laboratory infection. They showed that the behavioural effects differ depending on the *T. gondii* strain. The well-known effect of the “fatal attraction”, i.e. conversion of the innate fear of rodents of cat odours into an attraction to them, was observed irrespective of *T. gondii* strain in all tested mice two months after the infection; however, seven months after the infection, only the mice infected with one of the tested *T. gondii* strains continued to be attracted to cat odours. Nevertheless, it should be reminded that, in the wild, only few mice survive longer than two months and consequently, the disappearance of the “fatal attraction” as well as, for example, prolongation of reaction times (Hrdá et al. 2000) several months after the infection, is likely to have no serious effect on the fitness of *T. gondii*.

What I miss in the present special issue of *Folia Parasitologica*? First of all, I miss some study or a review

concerning the effects of *T. gondii* on the reproduction of humans and mice. The effect of latent toxoplasmosis on the embryonic growth rate was reported about five years ago (Flegr et al. 2005a) and was confirmed by another large-scale study two years later (Kaňková and Flegr 2007). Similarly, an increased probability of male offspring in both humans (Kaňková et al. 2007a) and mice (Kaňková et al. 2007b) is a potentially important phenomenon that could and should be easily studied using the already available data from any obstetrical or gynaecological service. The phenomenon of the protective effects of Rh blood group positivity against certain effects of latent toxoplasmosis has been recently reported (Flegr et al. 2008c, Novotná et al. 2008, Flegr et al. 2009). However, it is certainly worthwhile to try to find whether Rh-positivity protects not only against deterioration of psychomotor performance but also against other toxoplasmosis-induced effects, including the psychiatric symptoms. I also miss studies about possible links between toxoplasmosis and suicide as suggested last year (Arling et al. 2009) and between latent toxoplasmosis and Parkinson’s disease, a new phenomenon recently studied by two Turkish groups (Celik et al. 2010, Miman et al. 2010). We have to look forward to the next special issue or possibly a monograph devoted to the interesting topic of toxoplasmosis-associated phenotypical effects.

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