



Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres



Letter to the Editor

Toxoplasmosis, but not borreliosis, is associated with psychiatric disorders and symptoms



Keywords:

Incidence
Risk factors
Etiology
Infection hypothesis
Schizophrenia
Autism
OCD
Major depression

Dear Editors,

Infection by the parasite *Toxoplasma*, which affects about 33% of world population, is associated with increased risk of several mental health disorders, the most strongly with schizophrenia (Torrey et al., 2007; Torrey et al., 2012; Yolken et al., 2017). It is, however, unknown whether toxoplasmosis really plays a special role in the etiopathogenesis of these disorders and whether schizophrenia is associated with this infection the most strongly, or whether this association has just been the most intensively studied for historical reasons. We used the data from 46,000 subjects, 3440 tested for toxoplasmosis and 7800 for borreliosis, who took part in an internet survey primarily focused on effects of toxoplasmosis on human sexual behavior (Flegr and Kuba, 2016); for searching for the associations of these infections with 22 mental health disorders and other indices of impaired mental health – see (Flegr and Horacek, 2017) for technical details and <https://doi.org/10.6084/m9.figshare.5593288> for the data.

The Supplementary Tables 1 and 2 show the association of *Toxoplasma* and *Borrelia* infections with the incidence of particular disorders. The typical toxoplasmosis-associated disorders were autism (OR = 4.86), schizophrenia (OR = 3.34), attention deficit hyperactivity disorder (OR = 3.02), Asperger syndrome (OR = 2.49), antisocial personality disorder (OR = 1.81), obsessive compulsive disorder (OR = 1.69), and general anxiety disorder (OR = 1.57). Borreliosis was associated only with major depression (OR = 1.65). ANCOVA tests with independent variables of age, sex and either toxoplasmosis or borreliosis showed that *Toxoplasma*-seropositive subjects, especially women, reported more serious problems with depression ($p = 0.042$), and anxiety ($p = 0.003$), while no effect of *Borrelia*-seropositivity was significant. Toxoplasmosis positively correlated with the intensity of suffering from diagnosed mental health disorders ($p = 0.001$), the intensity of suffering from mental health disorders undiagnosed by doctors ($p = 0.003$), and with the number of different mental health disorders respondents checked on the list ($p < 0.0005$). These associations were weaker or absent for borreliosis: the intensity of suffering from diagnosed mental health disorders ($p = 0.005$), the intensity of suffering from undiagnosed mental health disorders ($p =$

0.796), and the number of different mental health problems ($p = 0.121$). In the *Toxoplasma*-free subjects, the number of mental health disorders in *Borrelia*-free and *Borrelia*-infected subjects did not differ while in the *Toxoplasma*-infected subjects this number was about two times higher in *Borrelia*-infected subjects (toxoplasmosis–borreliosis interaction: $p = 0.013$).

The Supplementary Table 3 illustrates the effects of the infections for the subset of 1997 raters reporting the results of the serological tests for both diseases. After the correction for multiple tests, toxoplasmosis had a significant effect on the intensity of symptoms of depression, anxiety, and obsessions. Borreliosis had a significant effect on anxiety, ($p = 0.037$, n.s. after the correction for multiple tests), and a borderline effect on depression ($p = 0.054$). Again, borreliosis was associated with higher depressive and anxiety symptoms only in *Toxoplasma*-seropositive subjects (Fig. 1); formally, however, the effects of the toxoplasmosis–borreliosis interaction on anxiety ($p = 0.080$) and depression ($p = 0.136$) were not significant.

Our study probably involves the largest ever population of *Toxoplasma*-tested participants – the usual size of populations in similar studies is at least one order of magnitude smaller. The study was exploratory and hypothesis-free in the sense that all main mental health disorders have been analyzed and all results, both positive and negative, have been reported. This approach remedies the well-known problems of the drawer and the cherry picking of artifacts – the problems of reporting only positive or “interesting” results of studies.

The largest limitation of the study was that the subjects self-reported their health status, including the incidences of particular disorders, as well as their infection status itself. This is a tradeoff for being able to study the interaction between acquired infections and mental health problems on a large enough sample. Our previous analyses of a sample of 3827 subjects who had been tested in our laboratory for *Toxoplasma* seropositivity and later registered as our internet volunteers showed that the information concerning toxoplasmosis is 99.5% correct (Flegr, 2017). Still, it is highly probable that some raters misreport their psychiatric diagnoses. The results of Monte Carlo modeling, however, showed that stochastic errors caused by misreporting health status can result only in false negative results of a study – the failure to detect existing associations, not false positive results of a study – detecting non-existing associations (Flegr and Horáček, 2017).

Given the cross-sectional design of this study, we cannot address the problem of causality. It is neither probable that mental health disorder could increase the risk of acquiring the infection, nor of reporting the *Toxoplasma* infection but not the *Borrelia* infection. However, it is possible that some unknown factor, such as immunodeficiency, could increase both the risk of mental health disorders and the *Toxoplasma* infections. In the light of already published data and our knowledge of the biology of the studied neuropathogens, however, the most parsimonious interpretation of the observed association is the positive effect of the infections on the rate of specific mental health disorders.

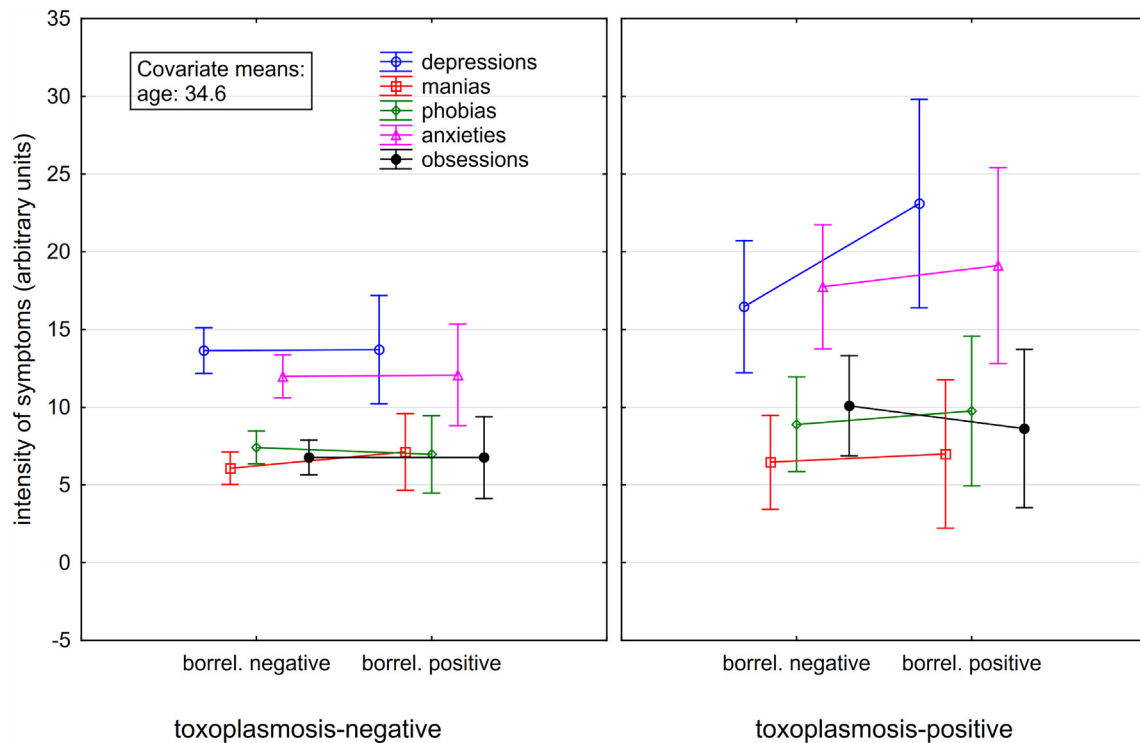


Fig. 1. Effects of *Toxoplasma*- and *Borrelia*-seropositivity on reported psychiatric symptoms. The spreads show 95% confidence intervals.

Results obtained in the study suggest that toxoplasmosis has strong correlation with the rate of several mental health disorders. Borreliosis showed only a weak association with major depression and with subjectively reported depressive and anxiety symptoms; these associations, however, seem to exist only in *Toxoplasma*-co-infected subjects. It is important to mention that the course of acute toxoplasmosis in immunocompetent subjects is mild and is considered insignificant from the clinical point of view, while the opposite is often true for borreliosis. Our results suggest that despite seemingly asymptomatic course of latent toxoplasmosis, *Toxoplasma* could play the privileged role in the etiology of mental disorders.

Conflicts of interests

The Authors have declared that there are no conflicts of interest in relation to the subject of this study.

Contributors

Dr. Jaroslav Flegr collected the data and performed the statistical analyses, both authors wrote and approved the final manuscript.

Acknowledgments

We would like to thank Lincoln Cline for her help with the final version of the paper.

Appendix A. Supplementary data

Supplementary data to this article (three tables and two figures) can be found online at <https://doi.org/10.1016/j.schres.2018.02.008>.

References

- Flegr, J., 2017. Predictors of *Toxoplasma gondii* infection in Czech and Slovak populations: the possible role of cat-related injuries and risky sexual behavior in the parasite transmission. *Epidemiol. Infect.* 145 (7), 1351–1362.
- Flegr, J., Horacek, J., 2017. Toxoplasmosis, but not Borreliosis, is Associated with Psychiatric Disorders: A Cross-sectional Survey on 46 Thousand of Subjects. *BioRxiv* <https://doi.org/10.1101/231803>.
- Flegr, J., Horáček, J., 2017. *Toxoplasma*-infected subjects report an obsessive-compulsive disorder diagnosis more often and score higher in obsessive-compulsive inventory. *Eur. Psychiatry* 40, 82–87.
- Flegr, J., Kuba, R., 2016. The relation of *Toxoplasma* infection and sexual attraction to fear, danger, pain, and sNeuropharmacologyubmissiveness. *Evol. Psychol.* 14 (3).
- Torrey, E.F., Bartko, J.J., Lun, Z.R., Yolken, R.H., 2007. Antibodies to *Toxoplasma gondii* in patients with schizophrenia: a meta-analysis. *Schizophr. Bull.* 33, 729–736.
- Torrey, E.F., Bartko, J.J., Yolken, R.H., 2012. *Toxoplasma gondii* and other risk factors for schizophrenia: an update. *Schizophr. Bull.* 38 (3), 642–647.
- Yolken, R., Torrey, E.F., Dickerson, F., 2017. Evidence of increased exposure to *Toxoplasma gondii* in individuals with recent onset psychosis but not with established schizophrenia. *PLoS Negl. Trop. Dis.* 11 (11).

Jaroslav Flegr

Division of Biology, Faculty of Science, Charles University in Prague, Prague, Viničná 7, 128 44, Czech Republic
Applied Neurosciences and Brain Imagination, National Institute of Mental Health, Klecany 250 67, Czech Republic
Corresponding author at: Division of Biology, Faculty of Science, Charles University in Prague, Prague, Viničná 7, 128 44, Czech Republic.
E-mail address: flegr@cesnet.cz

Jiří Horáček

Applied Neurosciences and Brain Imagination, National Institute of Mental Health, Klecany 250 67, Czech Republic
E-mail address: jiri.horacek@nudz.cz

16 January 2018