



Letter to the editor

Toxoplasmosis, but not borreliosis, is associated with psychiatric disorders and symptoms - false negative findings?


Dear Editor,

I read with interest the letter “Toxoplasmosis, but not borreliosis, is associated with psychiatric disorders and symptoms” (Flegr and Horacek, 2018). In this internet survey, borreliosis was associated only with major depression (OR = 1.65), but this effect became non-significant when controlling for age and sex. The absence of association between borreliosis and psychiatric disorders is interesting. *Borrelia burgdorferi* (Bb) is related to *Treponema pallidum*—the well-known cause of neuropsychiatric symptoms. Previous studies have reported association between borreliosis and mental health symptoms, suicide, psychiatric diagnoses and psychiatric hospitalizations (Fallon et al., 1993; Fallon and Nields, 1994; Hajek et al., 2002; Hajek et al., 2006; Bransfield, 2018; Koster and Garro, 2018). An epidemiological study compared the frequency of antibodies to Bb in a sample of 926 consecutive participants admitted for psychiatric hospitalization and 884 controls. In this study, seropositivity for Bb was significantly more frequent in the hospitalized participants relative to controls in both unmatched and sex and age matched samples. One-third of the psychiatric inpatients had serological signs of past Bb infection, as compared to 19% of controls (Hajek et al., 2002). Seropositive subjects were uniformly distributed among the studied psychiatric diagnostic categories, with none exhibiting stronger association with seropositivity (Hajek et al., 2006).

I believe that methodological reasons likely underlie the differences in results between the two large studies. The study by Flegr and Horacek (2018) used self-reports of both psychiatric and infectious disorders, whereas our previous study verified the psychiatric diagnosis by hospitalization and the exposure to Bb by serology. I agree with Flegr and Horacek, that relying on self-reports, especially for a difficult to diagnose condition such as Lyme borreliosis, could bias the findings.

In their Internet survey, Flegr and Horacek inquired whether participants were tested and if so, whether they did or did not have antibodies against Bb. Thus, they focused on seropositivity, not on the clinical diagnosis of Lyme borreliosis. Serological testing for Bb is more complex than testing for toxoplasmosis. It is frequently associated with both false positive and false negative results. Unlike testing for toxoplasmosis, it requires verification by western blot and alone is insufficient to diagnose Lyme borreliosis (Moore et al., 2016). In addition, Flegr and Horacek necessarily included participants tested in many different laboratories and they did not have information about which and how many tests were used. There are many kits for assessment of Bb,

which widely differ in their performance (Smismans et al., 2006; Cook and Puri, 2016). These issues introduce noise, may explain the stronger effect of toxoplasmosis and the absence of association between seropositivity for Bb and psychiatric morbidity, which was previously documented in a study, which worked with the actual serological results, all tests were done in a single laboratory (the National Reference Laboratory), using the best practices and standards and were verified by western blot in a proportion of participants (Hajek et al., 2002).

Furthermore, it is unclear, why participants in the Flegr and Horacek study knew about their history of toxoplasmosis, which is mostly asymptomatic and not routinely tested for? Indeed, the number of participants reportedly tested for antibodies against toxoplasma was much smaller than the number of participants who recalled serological testing for Bb (3440 versus 7800). Perhaps, the individuals who were tested for toxoplasmosis suffered from more severe forms of the infection or had complicating factors, such as immunosuppression or other infections/disorders, which prompted a more thorough testing. The potential bias towards more severe forms of toxoplasmosis or towards participants with other health concerns/complications, could explain the greater effect of toxoplasmosis than borreliosis. This sampling bias is just one of several issues which may arise when analyses are performed only on a small, non-random subgroup from a larger pool of participants. We do not know if these subsamples, i.e. 3440 and 7800 out of a total sample of 46,000 subjects, were representative of the whole population.

Last but not least, I agree that it is highly probable that some raters misreported their psychiatric diagnoses. The extent to which this happens would depend on the type of screening instrument and may be particularly high for an online checklist of mental health disorders, as used here. In any case, the authors suggest that stochastic errors caused by misreporting health status can result in false negative results of a study. Considering the above listed issues and biases, a false negative finding may also be the most parsimonious explanation for the absence of association between Bb and psychiatric morbidity in the Flegr and Horacek study.

Conflict of interest

Dr. Hajek has no conflict of interest to disclose.

Acknowledgement

N/A.

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23 August 2018