



Original article

Toxoplasma-infected subjects report an Obsessive-Compulsive Disorder diagnosis more often and score higher in Obsessive-Compulsive Inventory

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ABSTRACT

Background: Latent toxoplasmosis, the life-long presence of dormant stages of *Toxoplasma* in immunoprivileged organs and of anamnestic IgG antibodies in blood, affects about 30% of humans. Infected subjects have an increased incidence of various disorders, including schizophrenia. Several studies, as well as the character of toxoplasmosis-associated disturbance of neurotransmitters, suggest that toxoplasmosis could also play an etiological role in Obsessive-Compulsive Disorder (OCD).

Methods: The aim of the present cross-sectional study performed on a population of 7471 volunteers was to confirm the association between toxoplasmosis and OCD, and toxoplasmosis and psychological symptoms of OCD estimated by the standard Obsessive-Compulsive Inventory-Revised (OCI-R).

Results: Incidence of OCD was 2.18% ($n = 39$) in men and 2.28% ($n = 83$) in women. Subjects with toxoplasmosis had about a 2.5 times higher odds of OCD and about a 2.7 times higher odds of learning disabilities. The incidence of 18 other neuropsychiatric disorders did not differ between *Toxoplasma*-infected and *Toxoplasma*-free subjects. The infected subjects, even the OCD-free subjects, scored higher on the OCI-R.

Limitations: Examined subjects provided the information about their toxoplasmosis and OCD statuses themselves, which could result in underrating the strength of observed associations.

Conclusions: The results confirmed earlier reports of the association between toxoplasmosis and OCD. They also support recent claims that latent toxoplasmosis is in fact a serious disease with many impacts on quality of life of patients.

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1. Introduction

About one-third of the human population of developed countries have latent toxoplasmosis, i.e., they carry the dormant stage of the coccidian parasite *Toxoplasma gondii* in their immunoprivileged organs, e.g., brain, eyes, and testes, for the rest of their lives [1]. For a long time, latent toxoplasmosis was considered to be asymptomatic and therefore harmless for immunocompetent subjects. Within the past 15 years, more and more analytic studies show that *Toxoplasma*-infected subjects have higher incidences of certain disorders [2], especially neuropsychiatric disorders [3]. The strongest evidence for a direct etiological role of toxoplasmosis exists for schizophrenia. The association

between schizophrenia and toxoplasmosis has been reported in at least 50 studies, including some prospective longitudinal studies [4–6]. These longitudinal studies showed that *Toxoplasma* infection had preceded the onset of schizophrenia for 6–36 months [7]. The presence of genes for rate-limiting enzymes of dopamine synthesis in *Toxoplasma* genome [8] as well as their expression in the brain of an infected host [9,10] suggest that an increased concentration of this neurotransmitter could be responsible for the increased incidence of schizophrenia.

Increased brain levels of dopamine in conjunction with a disturbance in the concentration of serotonin is known to play an important role not only in schizophrenia, but also in Obsessive-Compulsive Disorder (OCD) [11]. OCD is a chronic, heritable, and debilitating neuropsychiatric disorder and its incidence in the general population is about three times higher than that of schizophrenia [12]. OCD is characterized by recurrent thoughts (obsessions) and repetitive behaviors (compulsions), the latter

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often reported to “neutralize” obsessions and reduce anxiety [13].

It has been documented by two case control studies [14,15] that OCD patients have higher seroprevalence of toxoplasmosis than *Toxoplasma*-free subjects. Based on these two studies the overall Odds Ratio (OR) for OCD was computed as 3.40 (CI₉₅ = 1.73–6.68) [6]. In addition, our ecological regression study performed on a set of 88 countries showed a strong correlation between the prevalence of toxoplasmosis and the Obsessive-Compulsive Disorder-related burden in European and especially in non-European countries [2]. The prevalence of toxoplasmosis explained 18 and 36% of the between-countries variability in OCD-related burden in Europe and outside Europe, respectively. Recently, another internet-based cross-sectional study was performed on a cohort of 2619 subjects tested for toxoplasmosis. This study was not primarily focused on the relation between toxoplasmosis and mental disorders; however, it also monitored the prevalence of certain mental health disorders, including OCD. The number of OCD patients in 2248 *Toxoplasma*-free subjects was 62 while in 371 *Toxoplasma*-infected subjects it was 15, suggesting that the OR is equal to 1.63 for women and to 1.73 for men [16].

1.1. Aims of the study

The present study had three aims: (1) to test whether *Toxoplasma*-infected subjects have a higher probability of reporting an OCD diagnosis, (2) to test whether *Toxoplasma*-infected subjects in a normal (non-clinical) population express a higher intensity of OCD symptoms, (3) to assess the specificity of the toxoplasmosis-mental health disorder association. For these purposes, a large-scale cross-sectional internet study on a cohort of 7471 normal subjects was carried out. In the confirmatory part of the study, we tested hypotheses 1 and 2, while in the exploratory part of the study we searched for an association between toxoplasmosis and 20 mental health disorders.

2. Methods

2.1. Participants and procedure

Subjects were invited to participate in the study using a Facebook-based snowball method [17]. An invitation to participate in “an experiment searching for associations between keeping dogs and cats and health status and personality of a subject” was posted on the wall of the Facebook page “Guinea pigs”, a page for people willing to take part in diverse psychological and psychopathological experiments (www.facebook.com/pokusnikralici) [18]. This community consists of people who understand Czech language, i.e. Caucasians of Czech and Slovak origin, of various ages, education levels, occupations, and places of residence. To keep the study blind and avoid possible bias, no form of the term toxoplasmosis or *Toxoplasma* was mentioned during the recruitment, not even in the Informed Consent form. This omission was approved by the Institutional Review Board (IRB). The participants were informed about the general aims of the study (to study the relations of keeping dogs and cats with health status and personality traits) on the first page of the questionnaire. They were also provided with the following information: “The questionnaire is anonymous and obtained data will be used exclusively for scientific purposes. Your cooperation in the project is voluntary and you can terminate it at any time by closing this web page. Please share the link to this questionnaire with your friends, for example on Facebook”. The share button was pressed by 906 participants, which resulted in data from a total of 7500 responders from 20th August 2014 to 23rd December 2015.

2.2. Serological tests for toxoplasmosis

Pregnant women are not subjected to obligatory testing for toxoplasmosis neither in Czechia, nor Slovakia. Some blood donors as well as subjects who were suspected of having acute or chronic toxoplasmosis were tested for the presence of anti-*Toxoplasma* antibodies in various clinical facilities. However, most of the women and nearly all of the men who know their *Toxoplasma*-infection status were tested for toxoplasmosis by us during systematic research of behavioral effects of latent toxoplasmosis, which has been running at the Faculty of Science for 20 years. Within the past 3 years, we have also regularly offered such testing to registered members of the “Guinea pigs” community 2–3 times a year; about 1000 of them have already been tested. The complement-fixation test, which determines the overall levels of IgM and IgG antibodies of particular specificity and Enzyme-Linked Immunosorbent Assays (ELISA) (IgG ELISA: SEVAC, Prague), were used to detect the toxoplasmosis status of the subjects. Only subjects with clearly positive results of CFT and IgG ELISA tests were diagnosed as *Toxoplasma*-infected (or conversely *Toxoplasma*-free).

In a similar study performed recently on the “Guinea pigs” population, we also asked the responders when they had been tested for toxoplasmosis. The results showed that *Toxoplasma*-free participants had been tested relatively recently (mode = 1 year, median = 3.0 years, mean = 5.4 years). The highest rate of infection is in early childhood in Czechia and Slovakia. Therefore, the fraction of subjects with negative tests who were *Toxoplasma*-infected at the time of our study was probably relatively low.

2.3. Electronic questionnaire

The questionnaire was distributed as a Qualtrics (Provo, UT) survey. Responders used a 5-point Likert scale (1: never, 2: minimally (1–2 times in life), 3: rarely, 4: from time to time, 5: very often), to rate their past contacts with six known or suspected toxoplasmosis-associated risk factors (eating or tasting raw meat, touching soil during gardening, eating root vegetables that were not washed properly, drinking water from suspicious sources like creeks, having sex without a condom with numerous people). The responders were asked about the size of the communities they grew up in (1: less than 1000 inhabitants, 2: 1–5 thousand inhabitants, 3: 5–50 thousand inhabitants, 4: 50–100 thousand inhabitants, 5: 100–500 thousand inhabitants, 6: more than 500 thousand inhabitants). The subjects were also asked to rate the intensity of their life-long contact with cats (definitive hosts of *Toxoplasma*) using a 7-point scale (1 – never, 2 – we kept a cat only in the past and only for a short time, 3 – we kept a cat only in the past but for a long time, 4 – we have one cat, 5 – we have two cats, 6 – we have three cats, 7 – we have more than three cats) and whether they are *Toxoplasma*-infected. They were reminded that *Toxoplasma* is “a parasite of cats, dangerous especially to pregnant women”. The response “I do not know, I am not sure” was set as a default answer which the responders could change by selecting either “No, I was tested by a doctor and the result of my laboratory tests was negative” or “Yes, I was tested by a doctor and I had antibodies against *Toxoplasma*”. The responders of our questionnaires had three options: they could complete any questionnaire absolutely anonymously, they could sign the finished questionnaire by a code obtained after the anonymous registration, or they could sign the finished questionnaire by a code obtained after the non-anonymous registration. When we checked the information about toxoplasmosis status provided in 190 signed questionnaires with the corresponding information in our records, we found a perfect (100%) agreement.

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