Toxoplasma gondii exposure in patients suffering from mental and behavioral disorders due to psychoactive substance use

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Abstract

Background: Toxoplasma gondii infection has been associated with psychiatric diseases. However, there is no information about the link between this infection and patients with mental and behavioral disorders due to psychoactive substance use.

Methods: We performed a case-control study with 149 psychiatric patients suffering from mental and behavioral disorders due to psychoactive substance use and 149 age- and gender-matched control subjects of the general population. We searched for anti-T. gondii IgG and IgM antibodies in the sera of participants by means of commercially available enzyme-linked immunoassays. Seroprevalence association with socio-demographic, clinical and behavioral characteristics in psychiatric patients was also investigated.

Results: Anti-T. gondii IgG antibodies were present in 15 (10.1%) of 149 cases and in 14 (9.4%) of 149 controls (P = 1.0). Anti-T. gondii IgM antibodies were found in 11 (7.4%) of the 149 cases and in 16 (10.7%) of the 149 controls (P = 0.31). No association of T. gondii exposure with socio-demographic characteristics of patients was found. Multivariate analysis of clinical and behavioral characteristics of cases showed that T. gondii seropositivity was positively associated with consumption of opossum meat (OR = 10.78; 95% CI: 2.16-53.81; P = 0.003) and soil flooring at home (OR = 11.15; 95% CI: 1.58-78.92; P = 0.01), and negatively associated with suicidal ideation (OR = 0.17; 95% CI: 0.05-0.64; P = 0.008).

Conclusions: Mental and behavioral disorders due to psychoactive substance use do not appear to represent an increased risk for T. gondii exposure. This is the first report of a positive association of T. gondii exposure with consumption of opossum meat. Further studies to elucidate the role of T. gondii infection in suicidal ideation and behavior are needed to develop optimal strategies for the prevention of infection with T. gondii.

Keywords: Toxoplasma gondii, Infection, Seroprevalence, Psychiatric patients, Psychoactive drug Abuse, Epidemiology, Mexico

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Background

Toxoplasma gondii infection is a common zoonotic infection all around the world [1]. Infection with T. gondii is usually acquired by ingesting water or food contaminated with parasite oocysts shed by cats or by ingestion of raw or undercooked meat containing parasite tissue cysts [2]. Less commonly, T. gondii infection has been associated with blood transfusion [3] or transplantation [4,5]. Although most T. gondii infected people shows no symptoms, some infected individuals may develop toxoplasmosis, which is a disease with involvement of eyes, lymph nodes and central nervous system [1,2,6]. Toxoplasmosis in immunocompromised patients may be a life-threatening disease [2,7]. In addition, congenital toxoplasmosis may occur after primary T. gondii infection during pregnancy [2,8,9].

Infection with T. gondii has been associated with some psychiatric disorders including schizophrenia [10-12], personality disorders [13], and obsessive-compulsive disorder [14]. However, the association of T. gondii infection with mental and behavioral disorders due to psychoactive substance use has not been studied. In a previous descriptive study in psychiatric patients, we found that 4 of 26 patients with mental and behavioral disorders due to psychoactive substance use had T. gondii antibodies [10]. However, the study design (cross-sectional) and the small sample size did not allow us properly assessing the association of infection and disease. Therefore, in the present study, we sought to determine the association of T. gondii infection with patients suffering from mental and behavioral disorders due to psychoactive substance use attended in the psychiatric hospital of Durango City, Mexico. Furthermore, the association of T. gondii infection with the socio-demographic, clinical and behavioral characteristics of the patients was also investigated.

Methods

Study design and study populations

We performed a case-control seroprevalence study in 149 patients suffering from mental and behavioral disorders due to psychoactive substance use (cases) and 149 people from the general population (controls) in Durango City, Mexico from November 2013 to August 2014. Inclusion criteria for the cases were patients suffering from mental and behavioral disorders due to psychoactive substance use attended in the Hospital of Mental Health “Dr. Miguel Vallecobueno” in Durango City, aged 18 years and older, and who voluntarily accepted to participate in the study. Gender was not a restrictive criterion for enrollment. Cases were 18-67 (mean = 36.01 ± 12.48) years old, and included 123 males and 26 females. Mental and behavioral disorders in the 149 patients studied were due to use of alcohol (F10) in 38 patients, use of cannabinoids (F12) in 8, use of sedative hypnotics (F13) in 7, use of cocaine (F14) in 1, use of other stimulants including caffeine (F15) in 3, use of tobacco (F17) in 10, and multiple drugs use and use of other psychoactive substances (F19) in 82. Exclusion criterion for the cases was presence of severe illness that impairs their decision to participate in the study. Control subjects were randomly selected from the general population in Durango City. Controls were recruited from homes, schools, work places and streets as previously described [15,16]. Controls were matched with cases by age (±1 year) and gender. Controls were 18-67 (mean = 36.03 ± 12.49) years old, and included 123 males and 26 females. There was no difference in age between cases and controls (P = 0.98).

Socio-demographic, clinical, and behavioral data in cases

Patients submitted a standardized questionnaire in order to obtain their socio-demographic, clinical, and behavioral characteristics. Socio-demographic data obtained included age, gender, birthplace, residence, educational level, occupation, and socioeconomic status. Items of clinical characteristics were health status, history of lymphadenopathy, blood transfusions, transplantation and surgeries, presence of frequent headache, dizziness, and impairments in vision, hearing, memory and reflexes. In female patients, obstetric history was also obtained. In addition, the area of attention (outpatients or inpatients), the psychiatric diagnosis, evolution time, presence of treatment, response to treatment, and history of aggressiveness, suicidal ideation and suicide attempt from the patients were recorded. Psychiatric diagnosis was based on the ICD-10 classification [17]. Behavioral data included contact with animals, foreign traveling, frequency of meat consumption, type of meat consumed (pork, beef, goat, lamb, boar, chicken, turkey, pigeon, duck, rabbit, venison, squirrel, horse, opossum, or other), consumption of raw or undercooked meat and dried or processed meat (ham, sausages or chorizo), drinking untreated water or unpasteurized milk, consumption of unwashed raw vegetables and fruits, frequency of eating away from home (in restaurants or fast food outlets), contact with soil (gardening or agriculture), and type of flooring at home.

Serological detection of T. gondii antibodies

Sera from participants were analyzed for anti-T. gondii IgG antibodies with the commercially available enzyme immunoassay kit “Toxoplasma IgG” (Diagnostic Automation Inc., Calabasas, CA, USA). This test allows determining the presence and levels of IgG antibodies. A positive result was considered when a value of equal to or higher than 8 IU/ml of specific anti-T. gondii IgG antibody was obtained. All sera were further analyzed for anti-T. gondii IgM antibodies by the commercially available enzyme immunoassay “Toxoplasma IgM” kit.
IgG antibodies were present in 15 (10.1%) of 149 cases and in 16 (10.7%) of the 149 controls (P = 0.31). Anti-T. gondii IgG antibodies were detected in 1 (3.8%) of 26 female cases and in 3 (11.5%) of 26 female controls (P = 0.60). While anti-T. gondii IgM antibodies were found in 11 (7.4%) of the 149 cases and in 16 (10.7%) of the 149 controls (P = 0.31). Anti-T. gondii IgG antibodies were detected in 14 (11.4%) of 123 male cases and in 11 (8.9%) of 123 male controls (P = 0.52). The frequency of high (>150 IU/ml) anti-T. gondii IgG antibody levels was similar in male (12/123: 9.8%) and female (1/26: 3.8%) cases (P = 0.46).

With respect to the socio-demographic characteristics in cases, none of the variables studied (age, gender, birthplace, residence, occupation, educational level and socio-economic status) had a P value ≤0.10 by bivariate analysis (Table 1).

Of the clinical characteristics in cases, seropositivity to T. gondii was not associated with the area of attention (outpatients or inpatients), psychiatric diagnosis, evolution time, response to treatment, presence of other diseases, history of lymphadenopathy, blood transfusions, transplantation and surgeries, presence of frequent headaches, dizziness, and impairments in vision, hearing, memory and reflexes, or obstetric history in women. In contrast, seropositivity to T. gondii was negatively associated with aggressiveness, suicidal ideation and suicide attempts by bivariate analysis (Table 2). The prevalence of high (>150 IU/ml) anti-T. gondii IgG antibody levels was also lower in patients with aggressiveness (5/99, 5.1%) than in those (8/50, 16%) without aggressiveness (P = 0.03), and in patients with suicide ideation (5/99, 5.1%) than in those (8/50, 16%) without suicide ideation (P = 0.03). The frequency of high (>150 IU/ml) anti-T. gondii IgG antibody levels was lower (but not statistically significant) in patients with suicide attempt (2/57, 3.5%) than in those (11/92, 12%) without suicide attempt (P = 0.13).

A selection of behavioral variables in cases and controls and their association with T. gondii seropositivity is shown in Table 3. Of the behavioral characteristics in cases, the variables cats in the neighborhood, dogs at home, consumption of meat from boar, duck, opossum, and armadillo, eating unwashed raw vegetables, and soil flooring at home had P values ≤0.10 by bivariate analysis. Other behavioral characteristics including cats at home, cleaning cat excrement, traveling, consumption of pork, beef, venison, lamb, or meat from goat, chicken, turkey, pigeon, or squirrel, frequency of meat consumption, consumption of dried or processed meat, drinking unpasteurized milk or untreated water, consumption of unwashed raw fruits, and contact with soil had P values >0.10. Multivariate analysis of clinical and behavioral characteristics of cases with P values ≤0.10 in the bivariate analysis showed that seropositivity to T. gondii was positively associated with consumption of opossum meat.
and negatively associated with suicidal ideation (OR = 0.17; 95% CI: 0.05-0.64; P = 0.008). The result of the Hosmer-Lemeshow test (P = 0.96) indicated a good fit of our regression model.

**Discussion**

There are no reports on the association of *T. gondii* infection with mental and behavioral disorders due to psychoactive substance use. Therefore, through an age- and gender matched case-control study design we sought to determine such association in patients attended in a psychiatric hospital in northern Mexico. The seroprevalence of anti-*T. gondii* IgG and IgM antibodies and anti-*T. gondii* antibody levels were similar in patients than in the general population. Thus, our results suggest that mental and behavioral disorders due to psychoactive substance use are not associated with infection with *T. gondii*. Whether *T. gondii* infection might predispose to drug use or whether drug use might predispose to *T. gondii* infection is unknown. The 10.1% seroprevalence of *T. gondii* infection found in patients suffering from mental and behavioral disorders due to psychoactive substance use is comparable to the 7.4% seroprevalence of *T. gondii* infection reported in healthy blood donors in Durango City [18] but it is lower than that (21.1%) reported in waste pickers [19] and inmates [20]. Differences

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**Table 1 Socio-demographic characteristics of psychiatric patients with psychoactive substance use and seroprevalence of *T. gondii* infection**

| Characteristic                              | Subjects tested | Prevalence of *T. gondii* infection | P value |
|--------------------------------------------|-----------------|-------------------------------------|---------|
|                                            | No.             | No. | %    |       |
| Age groups (years)                         |                 |     |      |       |
| 30 or less                                 | 51              | 3   | 5.9  | 0.33   |
| 31-50                                      | 73              | 10  | 13.7 |       |
| >50                                        | 25              | 2   | 8.0  |       |
| Sex                                        |                 |     |      |       |
| Male                                       | 123             | 14  | 11.4 | 0.47   |
| Female                                     | 26              | 1   | 3.8  |       |
| Birth place                                |                 |     |      |       |
| Durango State                              | 126             | 11  | 8.7  | 0.25   |
| Other Mexican state or abroad              | 23              | 4   | 17.4 |       |
| Residence                                  |                 |     |      |       |
| Durango State                              | 142             | 15  | 10.6 | 1      |
| Other Mexican state                        | 7               | 0   | 0.0  |       |
| Residence area                             |                 |     |      |       |
| Urban                                      | 121             | 13  | 10.7 | 0.58   |
| Suburban                                   | 22              | 1   | 4.5  |       |
| Rural                                      | 6               | 1   | 16.7 |       |
| Educational level                          |                 |     |      |       |
| No education                               | 2               | 0   | 0.0  | 0.2    |
| 1-6 years                                  | 37              | 7   | 18.9 |       |
| 6-12 years                                 | 90              | 6   | 6.7  |       |
| >12 years                                  | 20              | 2   | 10.0 |       |
| Occupation                                 |                 |     |      |       |
| Laborer                                    | 96              | 11  | 11.5 | 0.57   |
| No laborer                                 | 53              | 4   | 7.5  |       |
| Socio-economic level                       |                 |     |      |       |
| Low                                        | 55              | 4   | 7.3  | 0.63   |
| Medium                                     | 93              | 11  | 11.8 |       |
| High                                       | 1               | 0   | 0.0  |       |
### Table 2 Clinical characteristics of psychiatric patients with psychoactive substance use and seroprevalence of *T. gondii* infection

| Characteristic                                      | Subjects tested | Prevalence of *T. gondii* infection | P value |
|----------------------------------------------------|-----------------|-------------------------------------|---------|
|                                                    | No.             | No. | %    |         |
| Patient group                                      |                 |     |      |         |
| Inpatients                                         | 98              | 12  | 12.2 | 0.22    |
| Outpatients                                        | 51              | 3   | 5.9  |         |
| Psychiatric diagnosis                              |                 |     |      |         |
| F10 (use of alcohol)                               | 38              | 3   | 7.9  | 0.89    |
| F12 (use of cannabinoids)                         | 8               | 1   | 12.5 |         |
| F13 (use of sedative hypnotics)                    | 7               | 1   | 14.3 |         |
| F14 (use of cocaine)                              | 1               | 0   | 0.0  |         |
| F15 (use of other stimulants, caffeine)            | 3               | 1   | 3.3  |         |
| F17 (use of tobacco)                               | 10              | 1   | 10.0 |         |
| F19 (use of multiple drugs)                        | 82              | 8   | 9.8  |         |
| Subtype of disorder                                |                 |     |      |         |
| F1x.0 (acute intoxication)                         | 2               | 0   | 0.0  | 0.87    |
| F1x.1 (harmful use)                                | 28              | 2   | 7.1  |         |
| F1x.2 (dependence syndrome)                        | 118             | 13  | 11.0 |         |
| F1x.5 (psychotic disorder)                         | 1               | 0   | 0.0  |         |
| Evolution time                                     |                 |     |      |         |
| <10 years                                          | 79              | 7   | 8.9  | 0.8     |
| 10-20 years                                        | 48              | 5   | 10.4 |         |
| >20 years                                          | 22              | 3   | 13.6 |         |
| Response to treatment                              |                 |     |      |         |
| Good                                               | 85              | 8   | 9.4  | 0.93    |
| Regular                                            | 53              | 6   | 11.3 |         |
| Bad                                                | 11              | 1   | 9.1  |         |
| Other psychiatric disease                          |                 |     |      |         |
| Yes                                                | 77              | 10  | 13.0 | 0.22    |
| No                                                 | 72              | 5   | 6.9  |         |
| Aggressiveness                                     |                 |     |      |         |
| Yes                                                | 99              | 6   | 6.1  | 0.02    |
| No                                                 | 50              | 9   | 18.0 |         |
| Suicide ideation                                   |                 |     |      |         |
| Yes                                                | 99              | 5   | 5.1  | 0.004   |
| No                                                 | 50              | 9   | 18.0 |         |
| Suicide attempt                                    |                 |     |      |         |
| Yes                                                | 57              | 2   | 3.5  | 0.03    |
| No                                                 | 92              | 13  | 14.1 |         |
| Number of suicide attempts                         |                 |     |      |         |
| 1-3                                                | 45              | 2   | 4.4  | 1       |
| >3                                                 | 12              | 0   | 0.0  |         |
| Time of last suicide attempt                       |                 |     |      |         |
| <6 months ago                                      | 26              | 1   | 3.8  | 1       |
| ≥6 months ago                                      | 31              | 1   | 3.2  |         |
Table 3 Bivariate analysis of selected putative risk factors for infection with *T. gondii* in psychiatric patients with psychoactive substance use and controls

| Characteristic                        | Patients tested | Prevalence of *T. gondii* infection | Controls tested | Prevalence of *T. gondii* infection | P value |
|---------------------------------------|----------------|-------------------------------------|----------------|-------------------------------------|---------|
|                                       | No. | No. | %    | No. | No. | %    |                              |
| Cats at home                          |     |     |      |     |     |      |                              |
| Yes                                   | 83  | 11  | 13.3 | 74  | 9   | 12.2 | 0.25                         |
| No                                    | 66  | 4   | 6.1  | 75  | 5   | 6.7  |                              |
| Cats in the neighborhood              |     |     |      |     |     |      |                              |
| Yes                                   | 99  | 13  | 13.1 | 119 | 12  | 10.1 | 0.73                         |
| No                                    | 50  | 2   | 4    | 30  | 2   | 6.7  |                              |
| Dogs at home                          |     |     |      |     |     |      |                              |
| Yes                                   | 124 | 15  | 12.1 | 121 | 11  | 9.1  | 0.72                         |
| No                                    | 25  | 0   | 0    | 28  | 3   | 10.7 |                              |
| Birds at home                         |     |     |      |     |     |      |                              |
| Yes                                   | 72  | 10  | 13.9 | 50  | 5   | 10   |                              |
| No                                    | 77  | 5   | 6.5  | 99  | 9   | 9.1  |                              |
| Traveled abroad                       |     |     |      |     |     |      |                              |
| Yes                                   | 55  | 3   | 5.5  | 52  | 5   | 9.6  | 1                            |
| No                                    | 94  | 12  | 12.8 | 97  | 9   | 9.3  |                              |
| Boar meat consumption                 |     |     |      |     |     |      |                              |
| Yes                                   | 34  | 6   | 17.6 | 22  | 0   | 0    | 0.22                         |
| No                                    | 115 | 9   | 7.8  | 127 | 14  | 11   |                              |
| Pigeon meat consumption               |     |     |      |     |     |      |                              |
| Yes                                   | 30  | 5   | 16.7 | 23  | 4   | 17.4 | 0.23                         |
| No                                    | 119 | 10  | 8.4  | 125 | 10  | 8    |                              |
| Duck meat consumption                 |     |     |      |     |     |      |                              |
| Yes                                   | 33  | 7   | 21.2 | 24  | 5   | 20.8 | 0.05                         |
| No                                    | 116 | 8   | 6.9  | 125 | 9   | 7.2  |                              |
| Opossum meat consumption              |     |     |      |     |     |      |                              |
| Yes                                   | 10  | 5   | 50   | 2   | 1   | 50   | 0.18                         |
| No                                    | 139 | 10  | 7.2  | 147 | 13  | 8.8  |                              |
| Armadillo meat consumption            |     |     |      |     |     |      |                              |
| Yes                                   | 10  | 5   | 50   | 4   | 1   | 25   | 0.32                         |
| No                                    | 139 | 10  | 7.2  | 145 | 13  | 9    |                              |
| Iguana meat consumption               |     |     |      |     |     |      |                              |
| Yes                                   | 14  | 3   | 21.4 | 5   | 1   | 20   | 0.39                         |
| No                                    | 135 | 12  | 8.9  | 144 | 13  | 9    |                              |
| Degree of meat cooking                |     |     |      |     |     |      |                              |
| Raw or undercooked                    | 11  | 2   | 18.2 | 20  | 2   | 10   | 1                            |
| Well done                             | 138 | 13  | 9.4  | 127 | 12  | 9.4  |                              |
| Unwashed raw vegetables               |     |     |      |     |     |      |                              |
| Yes                                   | 53  | 2   | 3.8  | 48  | 4   | 8.3  | 1                            |
| No                                    | 96  | 13  | 13.5 | 101 | 10  | 9.9  |                              |
in contributing factors for infection among the groups may explain the differences in the seroprevalences. Altogether, results indicate that mental and behavioral disorders due to psychoactive substance use do not predispose to infection with *T. gondii*. In contrast, high seroprevalence (18.2%) of *T. gondii* infection has been reported in psychiatric patients [10], and therefore, the low seroprevalence (10.1%) found in the present study was unexpected. Reported contributing factors for *T. gondii* infection in psychiatric patients include sexual promiscuity, consumption of unwashed raw fruits, and history of surgery [10]. These factors were not associated with *T. gondii* infection in the present study. The underlying mechanisms mediating a potential association of *T. gondii* infection with mental and behavioral disorders due to psychoactive substance use have not been elucidated. Infection with *T. gondii* may lead to behavioral changes in humans and animals and these changes have been reviewed recently [21,22]. The seroepidemiology of *T. gondii* infection among drug addicts has been poorly explored. Seroprevalence of *T. gondii* infection in intravenous drug addicts was 7.7% in Vietnam [23] and 47.6% in Spain [24]. However, these studies did not provide information about a correlation of *T. gondii* infection with mental and behavioral disorders due to psychoactive substance use.

We assessed a number of putative risk factors for *T. gondii* exposure. However, none of the socio-demographic characteristics of patients was associated with *T. gondii* seropositivity. In contrast, multivariate analysis showed that *T. gondii* exposure was positively associated with consumption of opossum meat and living in a house with soil flooring. The epidemiological link of consumption of opossum meat and *T. gondii* exposure is highly feasible since 16.6% of native opossums (*Didelphis virginiana*) in Durango were found positive for anti-*T. gondii* antibodies by using the modified agglutination test [25]. In addition, seropositivity to *T. gondii* has been found in several species of opossums [26]. Recently, isolation of *T. gondii* was obtained in a black-eared opossum (*Didelphis aurita*) from Brazil [27]. Of note, seroprevalence of *T. gondii* infection was also associated with consumption of armadillo meat by bivariate analysis. However, this association did not resist the multivariate analysis. On the other hand, the association of *T. gondii* seropositivity with living in a house with soil flooring found in the present study confirms previous observations in pregnant women in urban [28] and rural [29] Durango, Mexico. A contamination of soil floors at home with parasite oocyst might have occurred in these cases.

Of the clinical characteristics, *T. gondii* exposure was not associated with any specific type or subtype of mental and behavioral disorders due to psychoactive substance use. Intriguingly, aggressiveness, suicidal ideation and suicide attempts were negatively associated with seropositivity to *T. gondii* by bivariate analysis. Further analysis by logistic regression showed that *T. gondii* exposure was negatively associated with suicidal ideation. This result was unexpected since *T. gondii* seropositivity has been associated with suicide attempts [30,31]. In a recent study in psychiatric patients in Durango City, we found an association of high anti-*T. gondii* IgG levels with suicide attempts [32]. It is not clear why *T. gondii* exposure was negatively associated with suicidal ideation in patients suffering from mental and behavioral disorders due to psychoactive substance use in this study. Differences in the populations among the studies might account for explaining the apparently conflicting results. Depression rate was higher in the previously studied population than in patients in the present study. In addition, in the previous study, we sampled patients with a number of psychiatric disorders while in the present study we only sampled patients suffering from mental and behavioral disorders due to psychoactive substance use. It raises a question whether psychoactive substance use influences the rate of suicide behavior in *T. gondii* infected patients. Remarkably, both *T. gondii* infection and psychotropic drugs influence the dopaminergic pathways. Infection with *T. gondii* has been associated with an increase in dopamine in brain [33]. Most drugs of abuse increase the dopamine neurotransmission [34]. In contrast, a reduced dopamine synthesis in marihuana users has been found [35]. On the other hand, dopamine and serotonin have been involved in suicide behavior.

### Table 3 Bivariate analysis of selected putative risk factors for infection with *T. gondii* in psychiatric patients with psychoactive substance use and controls (Continued)

| Untreated water | Yes | 122 | 10 | 8.2 | 0.15 | 96 | 10 | 10.4 | 0.77 |
|----------------|-----|-----|----|-----|------|----|----|------|------|
| No             | 27  | 5   | 18.5 | 53 | 4 | 7.5 |
| Floor at home  |     |     |      |     |     |     |     |      |      |
| Ceramic or wood| 76  | 5   | 6.6 | 0.009 | 61 | 5 | 8.2 | 0.72 |
| Concrete       | 66  | 7   | 10.6 | 81 | 8 | 9.9 |
| Soil           | 7   | 3   | 42.9 | 6 | 0 | 0 |
and aggression [36]. Therefore, alterations in neurotransmitters as dopamine due to *T. gondii* infection and substance use could be influencing the rate of aggressiveness and suicide behavior in our patients. Both substance use [37] and high levels of anti-*T. gondii* IgG antibodies [32] have been associated with suicide attempts in psychiatric patients in our region. However, the negative association of *T. gondii* infection with suicide ideation found in patients suffering from mental and behavioral disorders due to psychoactive substance use suggests a protective effect of *T. gondii* against suicide ideation in these patients. Interestingly, a negative effect of latent toxoplasmosis on the suicide-associated burden in non-European countries was recently reported [38]. Most of the studied patients in the current study used several drugs but marihuana use was common among them. It raises the question whether the reduced dopamine synthesis in marihuana users might be somewhat overcame for an increase in dopamine production by *T. gondii* resulting in normal levels of dopamine and low rates of suicide ideation. On the other hand, it is unknown whether an overproduction of dopamine by both *T. gondii* infection and some psychotropic substances might also lead to a reduction of suicide ideation rates. The role of *T. gondii* in the production of neurotransmitters and their interactions has been scantily studied. Apart from dopamine, other neurotransmitters might play a role in suicide behavior. Low cerebrospinal fluid concentrations of 5-hydroxyindolacetic acid has been associated with suicidal behavior [39,40]. Whether production of dopamine (and perhaps other neurotransmitters) by *T. gondii* is compensating excitatory or inhibitory effects of neurotransmitters associated with suicide behavior should be elucidated. Infections with *T. gondii* or HIV/*T. gondii* co-infections in intravenous drug users have correlated with altered serum cytokine levels including increased levels of TNF-α, IL-6 and IL-12 [41]. Further studies with a different study design to assess the negative association of *T. gondii* exposure with suicidal behavior in patients suffering from mental and behavioral disorders due to psychoactive substance use is needed.

In the present study, analysis of the association of *T. gondii* infection with the characteristics of the patients was based on results of anti-*T. gondii* IgG antibodies. In fact, anti-*T. gondii* IgG antibodies appear very early after infection [42]. Results of anti-*T. gondii* IgM antibodies were not included in the analysis because of a number of limitations for the diagnosis of *T. gondii* infection. Firstly, tests for detection of anti-*T. gondii* IgM antibodies may have a high rate of false positive results caused by limitations in test specificity [43]. Therefore, interpretation of the increased IgM seroprevalence found in the current study should be taken with care. Secondly, the absence of anti-*T. gondii* IgM in subjects with anti-*T. gondii* IgG antibodies indicates a chronic infection but the presence of the IgM marker does not necessarily indicate an acute infection. Anti-*T. gondii* IgM antibodies are detectable early after infection and can persist for prolonged periods of time after infection [2,43]. Therefore, seropositivity to IgM alone is not considered an acceptable diagnostic criterion for acute infection.

**Conclusions**

We conclude that infection with *T. gondii* is not associated with mental and behavioral disorders due to psychoactive substance use. This is the first report of a positive association of *T. gondii* exposure with consumption of opossum meat. Further studies to elucidate the role of *T. gondii* infection in suicidal ideation and behavior are needed to develop optimal strategies for the prevention of infection with *T. gondii*.

**Competing interests**

The authors declare that they have no competing interests.

**Authors’ contributions**

CAE conceived and designed the study protocol, performed the laboratory tests, analyzed the data, and wrote the manuscript. DCO, SJPV, MSJ, YAA and IBG obtained the blood samples and clinical data, and/or performed the data analysis. JHT, LFSA and OL performed the data analysis and wrote the manuscript. MNOJ obtained the clinical data and performed the data analysis. All authors read and approved the final version of the manuscript.

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