



Mental Health and Latent Toxoplasmosis: Comparison of Individuals with and without Anti-*Toxoplasma* Antibodies



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Abstract

Aim: There is evidence to suggest that the protozoan *Toxoplasma gondii* affects the mental health of people who are infected with it. The aim of the present study was to examine the relationship between *T. gondii* and mental health.

Methods: A total of 200 students (87 men and 113 women) of Jundishapur University of Medical Sciences (Ahvaz, Iran) were tested for the presence of anti-*Toxoplasma* antibodies and completed the General Health Questionnaire (see Appendix 1, available at: <http://www.longwoods.com/content/24938>) and a demographic form. Data were analyzed using independent samples t-test, chi-square test and Fisher's exact test.

Results: Infected women had significantly lower scores in somatic symptoms ($p = 0.04$), anxiety/insomnia ($p = 0.006$) and depression ($p = 0.04$) compared with non-infected women. Difference in social dysfunction was not significant ($p > 0.05$). There were no significant differences in somatic symptoms, anxiety/insomnia, depression and social dysfunction between infected and non-infected men (all $p > 0.05$).

Conclusion: Our findings indicate that latent toxoplasmosis can affect some components of mental health just in women.

Introduction

Toxoplasmosis is one of the most common parasitic infections caused by the obligate intracellular protozoan parasite *Toxoplasma gondii* (Dubey 2010; Prandovszky et al. 2011; Suzuki 2002). Humans and other warm-blooded vertebrates, including birds, livestock and marine mammals, can be infected by *T. gondii* (Dubey 2010; Prandovszky et al. 2011; Suzuki 2002). Humans are usually infected by consumption of undercooked or raw meat containing tissue cysts, vegetables contaminated with cat feces or contaminated drinking water (Herrmann, 2010; Kijlstra and Jongert, 2008). After a short phase of acute toxoplasmosis, the parasite encysts in the host muscle and central nervous system (particularly neurons and glial cells) and becomes latent probably throughout the host's lifetime (Dubey and Jones 2008; Miller et al. 2009; Prandovszky et al. 2011).

The parasite manipulates the behaviour of its intermediate host, increasing their transmission efficiency (Da Silva and Langoni

2009; Kristina and Fittipaldi 2008; Webster 2007). Animal studies have found distinct behavioural changes and cognitive dysfunction in infected rodents (Lamberton et al. 2008; Webster 2007; Webster et al. 2006). Some researchers also have reported psychotic symptoms (Hamidinejat 2010), changes in personality (Flegr and Havlicek 1999; Flegr and Tolarova 2000; Flegr et al. 1996; Novotná et al. 2005; Khademvatan et al. 2013) and neurological and psychiatric disorders (Arling et al. 2009; Brown et al. 2005; Cetinkaya et al. 2007; Gale et al. 2014; Hinze-Selch et al. 2007; Horacek et al. 2012; Kar and Misra 2004; Khademvatan 2014; Khademvatan et al. 2013, 2014; Mahmoud and Hasan 2009; Niebuhr 2008; Mortensen et al. 2007; Pearce et al. 2012; Xiao et al. 2010; Yuksel et al. 2008) in *T. gondii*-infected individuals.

Haloperidol (an antipsychotic drug) and valproic acid (a mood stabilizer), which are used in the treatment of some mental illnesses, have been revealed to prevent the development of behaviour changes related to *T. gondii* (Jones-Brando et al. 2003; Yuksel et al. 2008).

For years, scientists have been intrigued by the association between toxoplasmosis and mental disorders, including schizophrenia disorder (Brown et al. 2005; Cetinkaya et al. 2007; Hinze-Selch et al, 2007; Khademvatan et al. 2014; Khademvatan 2014; Mahmoud and Hasan 2009; Mortensen et al. 2007; Niebuhr 2008; Yuksel et al. 2008), mood disorders (Arling et al., 2009; Gale et al, 2014; Kar and Misra, 2004; Khademvatan et al. 2013; Pearce et al., 2012; Xiao et al. 2010), obsessive-compulsive disorder (Miman et al. 2010; Brynska 2001), etc., and controversial findings have been reported.

Because of poor hygiene, the prevalence of *T. gondii* is high in Iran (approximately 50% of the population) (Arbabi and Hooshyar, 2009; Khademvatan et al. 2013; Sadjjadi et al. 2001), and toxoplasmosis continues to be a public health problem. Therefore, it is important to consider the possible consequences of this infection. The present study aimed to compare the mental health of students with and without latent toxoplasmosis.

Methods

Research was conducted over a period of 12 months from 2015 to 2016. A total of 222 students (101 men and 121 women) of Ahvaz Jundishapur University of Medical Sciences (in Ahvaz, Southwest Iran) voluntarily participated in the study and gave informed consent.

Before serological analysis, 22 individuals (14 men and 8 women) were excluded from the study, because either they failed to complete questionnaires or decided to withdraw from the study. Finally, 200 individuals (87 men and 113 women) remained in the study.

The study was approved by the ethical committee of the university (No: ETH-160). A 5-mL blood sample was taken from each subject for serological analysis. Also, each subject was asked to complete the Persian version of the General Health Questionnaire (GHQ) and a questionnaire to obtain

demographic data about ethnicity, gender, age, education, marital status and employment. Mean age of the subjects was 24.6 years (standard deviation = 4.3 years). The participants did not have any major psychiatric disorder, neurological disease or major physical disorder.

Serological test for toxoplasmosis

Blood samples were centrifuged at 3,000 rpm for 20 minutes to procure clear supernatants. The sera were kept at -20°C until the analysis. The immunoglobulin G (IgG) antibody levels in the two case and control groups were measured by the enzyme-linked immunosorbent assay technique (Torch-IgG, Trinity Biotech Company, USA) according to the manufacturer's instructions.

Questionnaires

GHQ was developed by Goldberg et al. (1978) to screen non-psychotic psychological disorders (Riahi and Izadi-Mazidi 2012). We used the 28-item version of the scale in the present study. Each item was rated on a four-point Likert scale (from 1 to 4).

The questionnaire consists of four sub-scales, each containing seven items, including somatic symptoms, anxiety/insomnia, social dysfunction and depression. All questions have the same weight.

The range of the reliability coefficients has been reported to be from 0.78 to 0.95 in various studies (Jackson et al. 2007).

There are significant correlations between the GHQ-28 and the Hospital Depression and Anxiety Scale and other measures of depression (Sterling 2011).

Statistical tests

Data were analyzed using multiple independent samples *t*-test, chi-square test and Fisher's exact test. The probability level of 0.05 was accepted as statistically significant. Statistical analyses were carried out using SPSS version 16.

Results

Serological analyses confirmed that 46 men (52.8%) and 50 women (44.2%) were seropositive and 41 men (47.1%) and 63 women (55.7%) were seronegative for *T. gondii* antibodies.

Frequencies of the participants' demographic characteristics and the distribution of latent toxoplasmosis according to the demographic variable are listed in Table 1.

Table 1. Distribution of latent toxoplasmosis according to demographic features

Demographic variable		Frequency N (%)		
		Total	IgG ⁺	IgG ⁻
Gender	Male	87 (43.5)	46 (52.87)	41 (47.12)
	Female	113 (56.5)	50 (44.24)	63 (55.75)
Marital status	Single	160 (80)	77 (48.12)	83 (51.87)
	Married	40 (20)	19 (47.5)	21 (52.5)
	Divorced/widowed	0	0	0
Occupation status	Yes	53 (26.5)	26 (49.05)	27 (50.94)
	No	137 (73.5)	67 (48.9)	70 (51.09)

IgG = immunoglobulin G; IgG⁺ = IgG-positive; IgG⁻ = IgG-negative.

There were no significant differences between two groups of IgG-positive and IgG-negative individuals with respect to ethnicity ($p = 0.3$), marital status ($p = 0.5$), level of education ($p = 0.1$) and occupational status ($p = 0.3$).

The mental health of infected and non-infected subjects was compared using the independent samples *t*-test. There were significant differences between infected and non-infected women in somatic symptoms ($t = 2.01$, $p = 0.04$), anxiety/insomnia ($t = 2.7$, $p = 0.006$) and depression ($t = 1.9$, $p = 0.04$). Difference in social dysfunction was not significant ($t = 0.89$, $p = 0.3$) (Table 2).

Differences in somatic symptoms ($t = 1.9$, $p = 0.06$), anxiety/insomnia ($t = -0.3$, $p = 0.7$), social functioning ($t = 1.1$, $p = 0.2$) and depression ($t = -0.5$, $p = 0.5$) were not significant at $p < 0.05$ (Table 3).

Table 2. Comparison using independent samples *t*-test of mental health subscales in women according to seroprevalence

Mental health*	IgG ⁺ women (N = 50)		IgG ⁻ women (N = 63)		<i>t</i>	<i>p</i>
	M	SD	M	SD		
Somatic symptoms	13.22	3.71	11.84	3.52	2.01	0.04
Anxiety/insomnia	13.42	4.47	11.46	2.95	2.79	0.006
Social dysfunction	14.97	2.63	14.52	2.72	0.89	0.37
Depression	10.61	3.80	9.28	3.23	1.99	0.04

IgG = immunoglobulin G; IgG⁺ = IgG-positive; IgG⁻ = IgG-negative; M = mean; SD = standard deviation.

*Social impairment: questions 1–7; Anxiety: questions 8–14; Social dysfunction: questions 15–21; Depression: questions 22–28.

Table 3. Comparison using independent samples *t*-test of mental health subscales in men according to seroprevalence

Mental health*	IgG ⁺ men (N = 46)		IgG ⁻ men (N = 41)		<i>t</i>	<i>p</i>
	M	SD	M	SD		
Somatic symptoms	11.97	3.39	10.68	2.55	1.99	0.06
Anxiety/insomnia	12.29	3.82	12.56	4.08	-0.31	0.7
Social dysfunction	15.46	3.35	14.70	2.89	1.13	0.2
Depression	9.76	3.23	10.19	4.13	-0.54	0.5

IgG = immunoglobulin G; IgG⁺ = IgG-positive; IgG⁻ = IgG-negative; M = mean; SD = standard deviation.

*Social impairment: questions 1–7; Anxiety: questions 8–14; Social dysfunction: questions 15–21; Depression: questions 22–28.

Discussion

The present study was conducted to investigate the associations between mental health and toxoplasmosis. Mental health issues caused by latent toxoplasmosis have been the subject of some previous studies. The majority of these studies are confined to referral centres, whereas the subjects of the present study were selected from the general population.

The results of this study indicate significant differences between infected and non-infected women in anxiety/insomnia, somatic

symptoms and depression. According to our results, *T. gondii*-infected women experience higher levels of anxiety/insomnia, physical symptoms and depression.

The association we found between latent toxoplasmosis and anxiety in women is consistent with the result of the study conducted by Shirbazou et al. (2010), which showed higher levels of stress and anxiety in *T. gondii*-infected women. Fleger and Harvlicek (1999) also, in a study on personality profile of young women with latent toxoplasmosis, found higher levels of ergic tension (frustration, tension, being overwrought) in infected women compared with the control group.

The finding is in contrast to previous research in animal models showing anxiolytic-like behaviour in *T. gondii*-infected rodents (Berdoy et al. 2000). Moreover, the finding is inconsistent with the finding that women with latent toxoplasmosis did not experience anxiety in situations in which the women would be anxious (Flegr 2010).

The association between latent toxoplasmosis and depression that we found in women is in contrast to previous findings. The study conducted by Shirbazou et al. (2010) reports that women with latent toxoplasmosis did not have elevated depression symptoms compared with controls. Furthermore, other previous studies (Gale et al. 2014; Pearce et al. 2012) found no association between latent toxoplasmosis and major depression disorders.

In the current study, women with toxoplasmosis reported significant levels of physical symptoms that were probably because of their anxiety/insomnia and depression. However, we found no significant differences in mental health subscales between infected and non-infected men. The finding is inconsistent with the study conducted by Shirbazou et al. (2010), which suggested that *T. gondii*-infected men had more levels of anxiety and depression compared with non-infected men, and the result of a case report done by Kar and Misra (2004) that described a probable

association between toxoplasmosis and depression in a man.

There are some potential reasons for these results from existing literature. According to manipulation hypothesis, a parasite may alter host behaviour to facilitate its own transmission from the intermediate to the definitive host in order to complete its life cycle (Da Silva and Langoni 2009; Kristina and Fittipaldi 2008; Webster 2007). In explanation of the mechanism for these changes, some investigations have pointed to the changes in neurotransmitter levels that have been caused as a result of host immune response to *T. gondii*. Dopamine and other neurotransmitters such as serotonin have been considered in *T. gondii*-induced behavioural changes (Prandovszky et al. 2011). Dopamine plays an important role in the control of pleasure, motivation and cognition, movements and reward to stimuli (Prandovszky et al. 2011). It has also been discussed that toxoplasmosis probably increases blood cortisol levels and causes anxiety and stress (Shirbazou et al. 2011).

Our findings indicate higher burdens in women than men. Animal studies may explain the higher burdens in women. In the early stages of toxoplasmosis, higher levels of interferon-gamma are produced by the spleens of male mice compared with those of female mice. It helps male mice to control the parasite multiplication more rapidly (Prandota 2011). In the current study, no significant difference was found in prevalence of IgG levels between men and women ($p = 0.1$). However, Lindová et al. (2006) reported higher seroprevalence in male compared with female students. Also, Xiao et al. (2010) found higher prevalence in women than men. We also found no significant differences in prevalence by ethnicity and level of education.

Different results obtained from the studies of *T. gondii* and psychological conditions may be related to *T. gondii* genotypes. Various genotypes of *T. gondii* have different geographical replication and different neuropathogenic potentials (Khademvatan et al. 2014).

Conclusion

To conclude, the present study reports that infection with *T. gondii* is a risk factor for mental health problems in only females. Consequently, there is a need to plan adequate programs to control such infections.

Limitations

Our research has some limitations; participants were highly educated, which means that the findings should be generalized to people with different education levels with caution. Moreover, participation in the study was voluntary, which may limit the generalizability of the results to less motivated individuals. Researchers interested in studying this field should attempt to engage participants from diverse populations.

Defining toxoplasmosis infection by IgG might not be sufficient. For example, there may be some differences between subjects of acute and chronic toxoplasmosis infection. The infection status might be another important confounding factor.

Conflict of interest

The authors declare no conflict of interests.

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