
بسم الله الرحمن الرحیم

# Toxoplasmosis and mental disorders

Pro.Seyed hamzeh hosseini
Psychiatrist
shhosseini@mazums.ac.ir

The causative agent of toxoplasmosis–*Toxoplasma gondii* Nicolle et Manceux–was discovered**in 1909.**

*Toxoplasma* is an **intracellular parasite** and can affect different cells of mammals. **These protozoa are neurotropicagents**

Two types of toxoplasmosis in humans are known: ***the congenital form, the result of prenatal infection from a recently infected mother, and postnatal acquired toxoplasmosis.***

Postnatalacquired toxoplasmosis has two forms–**the transient acute toxoplasmosis,** which is characterized by numerous specific and non-specific symptoms, and **life-long latent toxoplasmosis**,which is asymptomatic from the clinical point of view in immunocompetent subjects.

Rarely, certain symptoms of acute toxoplasmosis persist for months and even years as so-called **chronic toxoplasmosis**

The prevalence of latent toxoplasmosis varies widely in different countries of the world, reaching **approximately 90%** in certain areas.

The seroprevalence of infection **is 25%-30%, on average**, in Western and Eastern Europe.

In the United States, an overalseroprevalence varied between **11% and 22.5%**

This evidence is founded on the fact that the main **neurobiological changes caused by latent T. gondii** infection in humans are consistent with the pathophysiology of neuropsychiatric diseases such as ***schizophrenia and mood disorders***

Furthermore, an experimental study has shown that T. gondii infection in mammalian dopaminergic cells repeatedly **raises dopamine-dependent K+ secretion.**

In the same study, staining the brains of infected rats with dopamine-specific antibodies resulted in **strong staining of cysteine-containing regions.**

**Tyrosine hydroxylase**, the limiting enzyme in dopamine production, was also found within intracellular cysts.

***The overall conclusion of this study was that ET plays an important role in increasing dopamine metabolism in neurons***

Indeed, the dopaminergic system plays a significant role in the etiology of **mood disorders and schizophrenia.**

The **dopamine hypothesis** in BD states that high levels of dopamine are found in the mania/hypomania phases,while decreasing levels of this neurotransmitter occur in
the **depressive phase**

**first** meta-analysis found a higher prevalence ofT. gondii antibodies in patients with schizophrenia than healthy controls (**odds ratio [OR] = 2.73).**

It should be pointed out that this review collected data from papers published since the 1950s across 17 countries, including countries in Asia and Eastern Europe, which were absent at the time from Western databases such as MEDLINE.

However, the authors did not consider **age an important confounding factor** for ET diagnosis

In addition, the **heterogeneity of strains and their geographical distribution** might play a role in disease burden,

Hinze-Selch D, Da¨ubener W, Eggert L, Erdag S, Stoltenberg R, Wilms S. A controlled prospective study of toxoplasma gondii infection in individuals with schizophrenia: beyond seroprevalence. Schizophr Bull. 2007;33:782-8.

**secound** meta-analysis replicated the association between schizophrenia and ET (OR = 2.74). Through the Egger test (p = 0.045),

these authors also identified a greater trend toward publishing studies in this scope, and their results indicated a significant difference between cases and controls.

Arias I, Sorlozano A, Villegas E, Luna JD, McKenney K, Cervilla J, et alInfectious agents associated with schizophrenia: a metaanalysis. Schizophr Res. 2011;136:128-36

**Third** meta-analysis of these disorders,[14] including papers published until 2013, also found an association between ET and **schizophrenia (adjusted OR [aOR] = 1.43) and included BD and addiction** in the research. When adjusted for the previously outlined publication bias,[13] the study found no significant difference between studies that did and did *not adjust for matched age as a confounding variable.*

Regarding BD, the authors found an overall association with no evidence for publication bias (OR = 1.52), which is consistent with previous studies, a**nd no association was found between major depressive disorder (MDD) and ET.**

Sutterland AL, Fond G, Kuin A, Koeter MW, Lutter R, van Gool T, et al. Beyond the association. Toxoplasma gondii in schizophrenia, bipolar disorder, and addiction: systematic review and meta-analysis.

Acta Psychiatr Scand. 2015;132:161-79.

# **Forth studies**Toxoplasmosis and mental disorders in the Russian Federation (with special reference to schizophrenia

**Table 1. Prevalence of latent toxoplasmosis in the male and female patients and controls.**

| Group | Patients | | | Controls | | | Odds ratio | $C.I._{95}$ | p-values |
|---|---|---|---|---|---|---|---|---|---|
| | Examined | Positive results | | Examined | Positive results | | | | |
| | | Absolute number | Percent (%) | | Absolute number | Percent (%) | | | |
| Men | 75 | 29 | 39% | 82 | 22 | 27% | 1.72 | 0.88–3.37 | 0.11 |
| Women | 80 | 33 | 41% | 70 | 17 | 24% | 2.19 | 1.08–4.43 | 0.03 |
| Total | 155 | 62 | 40% | 152 | 39 | 25% | 1.93 | 1.16–3.23 | 0.007 |

https://doi.org/10.1371/journal.pone.0219454.t001

Stepanova EV, Kondrashin AV, Sergiev VP, Morozova LF, Turbabina NA, et al. (2019) Toxoplasmosis and mental disorders in the Russian Federation (with special reference to schizophrenia). PLOS ONE 14(7): e0219454. https://doi.org/10.1371/journal.pone.0219454
https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0219454

# Table 2. Toxoplasmosis in Mentally Ill Patients in the USSR (1964, 1966, 1970).

| Source | Mental Disorders including Schizophrenia* | | Controls | |
|---|---|---|---|---|
| | Examined (n) | Positive (%) | Examined (n) | Positive (%) |
| Anisimova [26] | 24 | 19.2 | 178 | 5.0 |
| Moiseeva [27] | 858 | 27.9 | 128 | 7.0 |
| Orestenko [28] | 230 | 34.6 | 200 | 13.0 |
| Savonenko and Karmanova [29] | 224 | 9.2 | 227 | 0.0 |
| Mihalev [25] | 460 | 32.4 | 225 | 5.0 |
| Petrov and Skokova [30] | 202 | 31.1 | 183 | 9.2 |
| Betin [31] | 340 | 16.7 | 186 | 2.15 |
| Motavkina et al. [32] | 1504 | 10.1 | 160 | 2.6 |

* Number of schizophrenia cases greater than 50%

https://doi.org/10.1371/journal.pone.0219454.t002

Stepanova EV, Kondrashin AV, Sergiev VP, Morozova LF, Turbabina NA, et al. (2019) Toxoplasmosis and mental disorders in the Russian Federation (with special reference to schizophrenia). PLOS ONE 14(7): e0219454. https://doi.org/10.1371/journal.pone.0219454
https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0219454

The data illustrated well established trend of the association between toxoplasmosis and
schizophrenia in **study areas of the USSR** and it was in agreement with the results obtained in other countries abroad. It was shown that the seroprevalence of toxoplasmosis among ***patients with mental disorders was 2–3 times more frequent than among healthy persons***

**In Germany**, the prevalence of toxoplasmosis in conjunction with various mental disorders was 43%-50% compared to 3% among healthy persons;

**in Poland**, the prevalence was 51% compared to 25%;

**in Czechoslovakia**, the prevalence was 43% compared to 10%, respectively

**latest**Thirty-one studies were included, and the majority found an association between exposure to toxoplasmosis and schizophrenia or bipolar disorder (58.3 and 54.5% of the included papers, respectively), but not major depressive disorder.

they found no significant difference in mean quality scores between studies that corroborated and contradicted the association hypothesis for eitherschizophrenia or bipolar disorder.

Fernandes SM, Dias AR, Miranda-Scippa A. Association between exposure to toxoplasmosis and major psychiatric disorders: a systematic review. Braz J Psychiatry. 2020;00: 000-000. http://dx.doi.org/10.1590/1516-4446-2020-0904

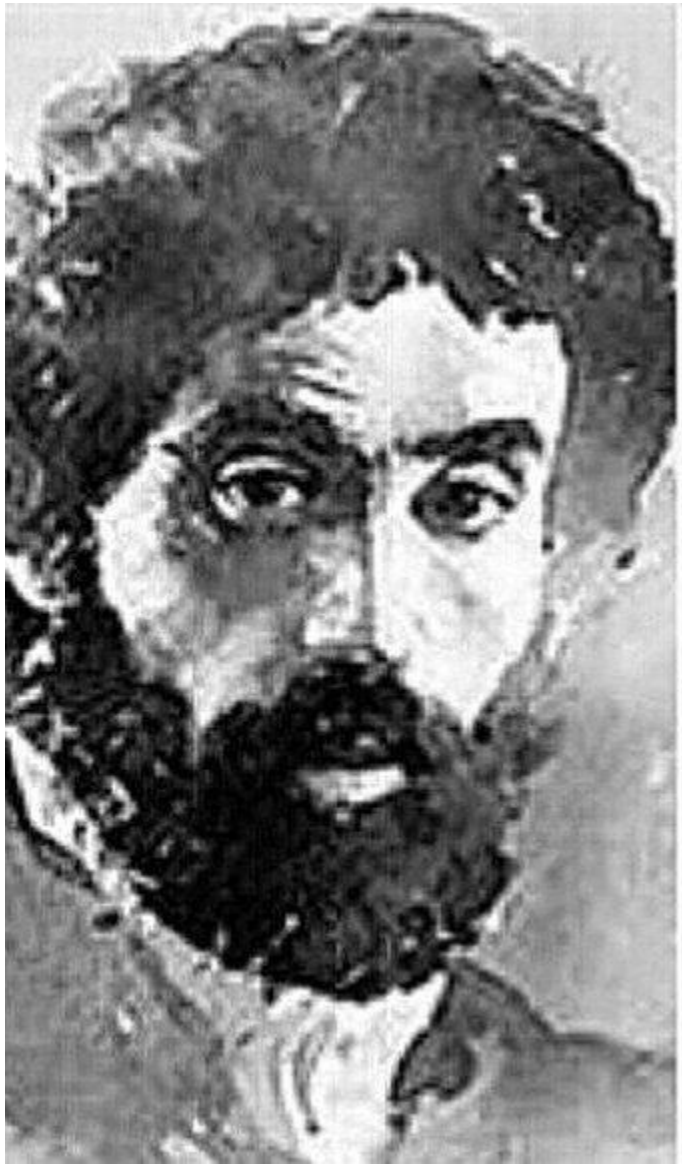
***Although there was no association between exposure to toxoplasmosis and major depressive disorder, the results indicate an association with both bipolar disorder and schizophrenia, despite their heterogeneity.***

***Further studies should be performed with more specific variables so that***
***the nature of these relationships can be elucidated***

In conclusion, The heterogeneity of the results demonstrates the need for greater attention to detail in future studies, including better defined samples and refined methods. While updating the state of art on research about the association between ET and major psychiatric disorders,

we suggest the inclusion of new variables in future studies: ***treatment status andserum antibody levels of T. gondii; the seroprevalence of other neurotropic pathogens (e.g., human immunodeficiency virus 1 and 2, cytomegalovirus, HSV 1 and 2, andhepatitis A, B, and C);*** a detailed description of the sample
regarding subtypes and different disease phases; and the neutralization of other confounders, such as age, gender, patients origin, and T. gondii strain.


از توجه شما متشکرم



من به آمار زمین مشکوکم تو چطور؟
اگر این سطح پر از آدمهاست
پس چرا اینهمه دلها تنهاست
بیخودی می گویند هیچکس تنهانیست
چه کسی تنهانیست؟ همه از هم دورند
همه در جمع ولی تنهایند
من که در تردیدم تو چطور؟
نکند هیچ کسی اینجانیست