



TOXOPLASMOSIS ASSOCIATION WITH PSYCHOSIS

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Abstract

The potential link between *Toxoplasma gondii* infection and psychosis—particularly schizophrenia and bipolar disorder—has become a central focus of interdisciplinary research spanning psychiatry, neurology, immunology, and infectious disease. Findings from epidemiological surveys, meta-analyses, and large-scale cohort studies suggest that *T. gondii* exposure, especially during prenatal or early developmental periods, may heighten susceptibility to psychotic disorders. Several biological mechanisms have been proposed, including neuroinflammation, immune dysregulation, dopaminergic imbalance, and gene–environment interactions. Despite broad evidence supporting this association, inconsistencies persist due to methodological limitations, strain variability, diagnostic heterogeneity, and regional differences in infection prevalence. The strongest support comes from longitudinal and registry-based studies that account for timing of infection and confounding factors, though definitive causality remains unproven. Most available research relies on seropositivity as an indirect marker of infection, restricting insights into temporal dynamics. Future investigations should integrate molecular parasite typing, host genetic and immune profiling, neuroimaging, and standardized diagnostic approaches. Interventional trials assessing antiparasitic or immunomodulatory therapies may further clarify clinical implications. Collectively, current evidence indicates that *T. gondii* may serve as an environmental risk factor in genetically predisposed individuals, underscoring the need to incorporate infectious exposures into models of psychosis pathogenesis.

Keywords: *Toxoplasma gondii*, psychosis, schizophrenia, Congenital Infection, Latent infection, psychiatric risk factors

INTRODUCTION

Toxoplasmosis, caused by the protozoan parasite *Toxoplasma gondii* (*T. gondii*), is one of the most common parasitic infections worldwide, affecting an estimated 30% to 50% of the global population [1]. While it often causes no symptoms in healthy people, it can lead to serious complications in those with weakened immune systems and in unborn babies. *T. gondii* has a complex life cycle with both sexual and asexual stages. Cats, especially domestic ones, are the main hosts, releasing infectious oocysts in their feces. Other animals, including birds, rodents, livestock, and humans, become infected by ingesting oocysts from contaminated water, soil, or food, or by eating undercooked meat containing tissue cysts [2]. After ingestion, oocysts release sporozoites that turn into tachyzoites, the fast-growing form that spreads throughout the body. The immune system usually controls this stage, causing the parasite to become bradyzoites, which form cysts in the brain and muscles [3]. These cysts can stay in the body for life and may reactivate if the immune system is weakened, such as in HIV patients or organ transplant recipients. *T. gondii* tends to target the brain and can cross the blood-brain barrier, raising concerns about its effects on brain function.

Recently, researchers have suggested a link between toxoplasmosis and mental illnesses, especially psychosis [4]. Psychosis involves symptoms like delusions, hallucinations, confused thinking, and losing touch with reality. It is a symptom seen in several psychiatric disorders, including schizophrenia, schizoaffective disorder, and bipolar disorder with psychotic features. Schizophrenia, one of the most studied psychotic disorders, affects about 0.3% to 0.7% of people worldwide during their lifetime [5]. Psychosis can have many causes, such as genetics, drug use, brain diseases, and infections, but the exact mechanisms are often unclear [6]. The dopamine hypothesis is a key theory that suggests too much dopamine activity in certain brain pathways causes positive symptoms like hallucinations, while reduced dopamine

function in the prefrontal cortex leads to negative and cognitive symptoms. Other brain chemicals, such as glutamate, GABA, and serotonin, also play roles [7]. Evidence supporting *T. gondii*'s role in psychosis comes from epidemiological, experimental, and clinical studies. Many large studies have found higher rates of *T. gondii* antibodies in people with schizophrenia compared to healthy individuals, indicating past infection [8,9]. Studies following children from birth suggest that prenatal exposure to *T. gondii* might increase the risk of developing schizophrenia later [10].

T. gondii may affect the brain in several ways. The parasite can produce enzymes similar to those that make dopamine in the host, raising dopamine levels in brain areas linked to psychosis. It also triggers activation of brain immune cells and the release of inflammatory molecules like IL-6, IL-1 β , and TNF- α , which can disrupt brain development and neurotransmitter balance seen in psychosis [11]. Animal studies show that rodents infected with *T. gondii* exhibit changes in behavior that resemble human psychiatric symptoms. These animals show less fear of predators, move more, and have memory problems, likely due to parasite-induced brain inflammation and neural changes [12]. These findings support the idea that *T. gondii* might contribute to mental illness and highlight the need for more clinical and laboratory research. Genetics add another layer of complexity. Certain gene variants related to immunity, brain chemicals, or brain development may increase the risk of psychosis in people infected with *T. gondii* [13]. This fits with the idea that schizophrenia results from a mix of genetic vulnerability and environmental factors. Differences in immune responses may also affect how strongly *T. gondii* impacts the brain, making the study of immune genetics important [14].

Maternal infection during pregnancy is a key risk factor. While congenital toxoplasmosis can cause serious brain damage, even mild infections in the mother may affect fetal brain development. This can disrupt key processes like neuron formation and brain wiring,

increasing the chance of psychiatric problems in later life [15]. Research by Khandaker et al. [16] supports the view that prenatal infections, including *T. gondii*, may raise the risk of psychosis. Recent brain imaging studies also show that people with schizophrenia who have *T. gondii* antibodies tend to have more loss of gray matter and damage to white matter, especially in areas that control thinking and emotions [17]. This suggests the parasite may contribute to brain changes seen in psychotic disorders.

Despite these findings, there are still many unanswered questions. It is not yet clear whether *T. gondii* directly causes psychosis, acts as a contributing factor, or simply marks people already at risk. Studies differ in methods, size, location, and parasite strains, which may explain inconsistent results. Most research has been cross-sectional, making it hard to determine cause and effect. Long-term studies are needed to see if *T. gondii* exposure comes before psychosis, especially in people with genetic risk. More research is also needed on how genes, environment, and immune responses interact to influence mental health after infection.

This research aims to address these gaps by bringing together evidence from epidemiological, clinical, and experimental studies on toxoplasmosis and psychosis. It will explore how the parasite might affect the brain through inflammation, chemical imbalances, and changes in development. By doing this, the paper highlights the importance of considering infections in psychiatric disorders and suggests directions for future research that could improve early diagnosis, prevention, and treatment for those at risk.

EPIDEMIOLOGY

Epidemiological studies strongly support a significant link between *Toxoplasma gondii* infection and psychosis. Many studies have shown that people exposed to *T. gondii* are more likely to develop psychotic disorders, including schizophrenia. For example, Sutterland et al. [18] conducted a meta-analysis and found that individuals with schizophrenia

were 2.7 times more likely to test positive for *T. gondii* IgG antibodies than healthy people. Similarly, a large case-control study by El-Sayed et al. [19] found much higher rates of *T. gondii* infection among schizophrenia patients compared to the general population. Other research has shown that the chance of *T. gondii* exposure is especially high in people with recent-onset psychosis compared to those with chronic schizophrenia, suggesting the infection might trigger psychotic episodes in those who are vulnerable [20].

Studies from different parts of the world also support this connection. For instance, research in China found higher rates of *T. gondii* exposure among patients with psychotic symptoms than in control groups, supporting the idea of a consistent global trend [17]. In addition, areas with higher rates of *T. gondii* infection tend to report more cases of psychotic disorders, indicating a wider public health concern.

New evidence points to the role of both genetic and environmental factors in this link. Some genes related to schizophrenia may become active due to *T. gondii* infection, increasing the risk of psychiatric illness [21]. Environmental stressors like early-life adversity or trauma may further increase this genetic risk, showing a complex interaction between biology and infection.

Clinical studies have noted that psychosis patients who test positive for *T. gondii* often have more severe cognitive problems, negative symptoms, and resistance to treatment. These findings not only suggest the parasite plays a role in causing psychosis but also that it may influence the illness's course and outcome [10]. The link between infection and symptom severity highlights the importance of considering infection history in psychiatric evaluations and the potential benefits of integrated care.

Long-term studies, such as those by Mortensen et al. [10], suggest that prenatal exposure to *T. gondii* raises the chance of developing schizophrenia later in life, indicating a possible effect of the parasite on brain development. Overall, epidemiological data strongly support

the connection between *T. gondii* infection and a higher risk of psychosis, emphasizing the need for further research to understand causality, underlying mechanisms, and potential treatments.

MECHANISMS OF INTERACTION

The connection between *Toxoplasma gondii* infection and psychosis is supported by several biological mechanisms that explain how this parasite might contribute to psychiatric symptoms. One well-studied mechanism is neuroinflammation. When *T. gondii* infects the brain, it activates immune cells like microglia and triggers the release of pro-inflammatory cytokines such as IL-6, TNF- α , and IFN- γ . These inflammatory substances can disrupt the blood-brain barrier, change synaptic communication, and lead to the neuronal problems often seen in psychotic disorders. Chronic brain inflammation may therefore play a key role in causing or worsening psychotic symptoms [22].

Another important mechanism involves the parasite's effect on neurotransmitters. *T. gondii* produces tyrosine hydroxylase, an enzyme essential for making dopamine. This can lead to higher dopamine levels in areas of the brain linked to schizophrenia. This fits with the dopamine hypothesis of psychosis, which suggests that too much dopamine activity contributes to symptoms of disorders like schizophrenia. Additionally, *T. gondii* infection has been linked to changes in serotonin and glutamate signaling, indicating broader imbalances in brain chemistry [23].

Genetic factors also seem to influence who develops psychosis after exposure to *T. gondii*.

Some people have gene variants affecting immune response or neurotransmission that make them more vulnerable to the infection's effects on the brain. These genetic risks may combine with environmental stresses, like trauma or early adversity, increasing the chance of developing psychosis following infection [21].

The immune system's role is another key factor. Abnormal immune responses, including higher levels of IL-1 β and IL-6, have been found in psychotic patients with a history of toxoplasmosis. These cytokines can interfere with brain development, affect the pruning of synapses, and alter neurotransmitter function, linking immune problems to psychotic symptoms [24].

Finally, prenatal exposure to *T. gondii* is linked to a higher risk of schizophrenia and related disorders later in life. The parasite may disrupt important brain development processes during pregnancy, such as neuron growth and migration. These changes could lead to brain abnormalities that show up as psychiatric disorders during adolescence or adulthood [25].

Overall, these mechanisms neuroinflammation, neurotransmitter changes, genetic vulnerability, immune system disruption, and altered brain development point to a complex model of how *T. gondii* might contribute to psychosis. This interplay between chronic infection and mental health highlights the need for ongoing research to better understand these pathways and develop effective treatments.

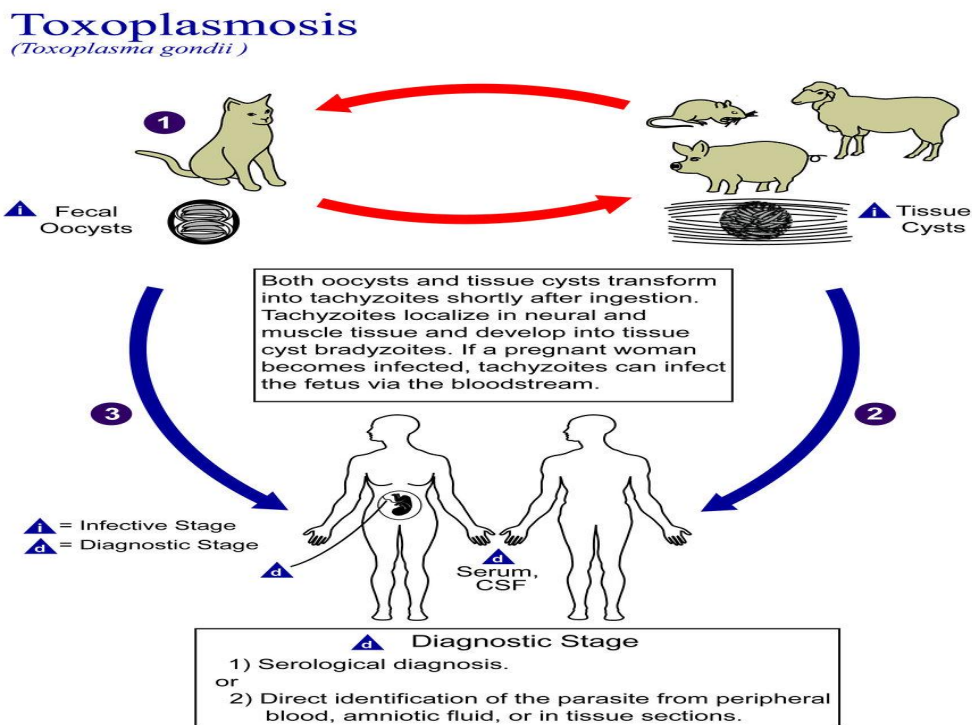


FIGURE 1: LIFE CYCLE OF *TOXOPLASMA GONDII*

This is an illustration of the life cycle of *Toxoplasma gondii*, the causal agent of Toxoplasmosis.
By: CDC/Alexander J. da Silva, PhD/Melanie Moser, Courtesy: Public Health Image Library.

TABLE 1: SUMMARY OF KEY STUDIES INVESTIGATING THE ASSOCIATION BETWEEN *TOXOPLASMA GONDII* INFECTION AND PSYCHOTIC DISORDERS

AUTHOR	TITLE	METHOD	RESULT	REMARK/FINDINGS
Liu et al [9]	Association between <i>Toxoplasma gondii</i> infection and psychiatric disorders: a cross-sectional study in China	5 ml of fasting blood was drawn from the subjects. The sample was centrifuged at 4000 r/min for 10 min, and then, the serum was separated for testing. Serological marker tests of <i>T. gondii</i> infection include anti-Toxoplasma IgM and IgG antibody measures using enzyme-linked immunosorbent assay (ELISA) (Auto Bio, China).	The positivity rate of anti-Toxoplasma IgM antibody in psychiatric patients was 0.23% (7/3101), while in the general population, it was 0.11% (2/1846), with no statistically significant difference between the two groups ($p = 0.359$).	This study compared various types of mental illness with the general population and found that compared to the general population, depression, recurrent depressive disorder, schizophrenia, and mania patients had a higher positivity rate of anti-Toxoplasma IgG antibody.
Fernandes et al. [27]	Association between exposure to toxoplasmosis and major psychiatric disorders: a systematic review	Immunofluorescence, chemiluminescence, enzyme-linked immunosorbent assay, enzyme immunoassays, or immune hemagglutination) and a diagnosis of schizophrenia,	Serological status of several neurotropic pathogens (i.e., cytomegalovirus, herpes simplex viruses HSV-1 and HSV-2, and <i>T. gondii</i>) in 722 newborns, of whom 198 were diagnosed with schizophrenia later in life and 524 were healthy controls. After controlling for gestational age, place and date of birth, age, and the mother's country of origin, there was a higher seroprevalence of both <i>T. gondii</i> and cytomegalovirus in the patient group (OR = 2.1; 95%CI 1.04,5 and OR = 2.2; 95%CI 1.0-5.1, respectively)	Serum antibody levels was also reported to be higher in patients with schizophrenia than healthy controls, and the acoustic startle response was slower in seropositive than seronegative individuals. These data are consistent with the psychomotor retardation observed in individuals seropositive for <i>T. gondii</i> who have not been diagnosed with a psychiatric disorder.
Cossu et al. [28]	Association between toxoplasmosis and bipolar disorder: A systematic review and meta-analysis	observational studies that compared seroprevalence of IgG class antibodies against <i>T. gondii</i> in patients with a diagnosis of bipolar disorder with healthy controls. We excluded studies that included <10 participants in each study arm and patients with a serious concomitant medical illness.	Overall, 23 studies were found with details about the proportion of cases with toxoplasmosis in samples of patients diagnosed with bipolar disorder and a comparison with healthy controls.	meta-analysis including 4021 patients diagnosed with bipolar disorder and 8669 healthy controls, extracted from 23 independent samples that the probability of being found positive for toxoplasmosis was higher in patients diagnosed with bipolar disorder than in healthy controls.

Campos-Carli et al. [29]	<i>Toxoplasma gondii</i> infection and chronic schizophrenia: is there any association?	Peripheral blood was drawn, and IgM and IgG anti- <i>T. gondii</i> antibodies evaluated by Enzyme-Linked Immunosorbent Assay (ELISA). Depressive, positive and negative symptoms assessed, respectively, by the Calgary Depression Scale (CDS) and the Positive and Negative Syndrome Scale (PANSS). Cognitive performance was assessed in patients by the Brazilian version of the Schizophrenia Cognition Rating Scale (SCoRS-BR).	The prevalence and titers of <i>T. gondii</i> IgM and IgG antibodies did not differ between patients and controls. The positive serology for <i>T. gondii</i> IgG antibodies was not associated with illness symptoms, cognitive performance, depressive symptoms or quality of life.	In conclusion, our data showed that <i>T. gondii</i> infection is not associated with schizophrenia. In addition, <i>T. gondii</i> seroprevalence and levels of IgG antibodies were not associated with demographic data, disease severity, depressive and cognitive symptoms and quality of life. Results might be influenced by strain-specific brain effects and high prevalence of <i>T. gondii</i> infection in sample. Further studies are needed in order to elucidate the role of <i>T. gondii</i> in schizophrenia pathophysiology.
Ansari-Lari et al. [30]	Association of <i>Toxoplasma gondii</i> infection with schizophrenia and its relationship with suicide attempts in these patients	Enzyme-linked immunosorbent assay (ELISA) was used. Data about demographic information in all subjects and duration of illness and history of suicide attempts in patients with schizophrenia were collected using a brief questionnaire and hospital records. Chi-square test and multivariable logistic regression were used for statistical analyses.	Among 99 cases, 42 individuals (42%) were positive for <i>T. gondii</i> antibody, vs. 41 (27%) among 152 controls (OR = 2, 95% CI: 1.2–3.4, P = 0.012). We compared the suicide attempts in patients with schizophrenia based on their <i>T. gondii</i> serologic status. There was a lower rate of suicide attempts in seropositive male patients than seronegative ones (OR = 0.3, 95% CI: 0.1–0.97, P = 0.04). Age of onset of schizophrenia did not differ between <i>T. gondii</i> -infected and non-infected patients.	A lower rate of suicide attempts in toxoplasma-infected male subjects than in non-infected men was observed. Therefore, in addition to gender difference, observed the relationship between <i>T. gondii</i> and suicide attempts in patients with schizophrenia in the opposite direction found in previous research. Gender differences in behavioural changes induced by latent toxoplasmosis were reported. A positive relationship between infection with <i>T. gondii</i> and schizophrenia in the present study was observed. Age of onset of disease did not show significant differences in our study. The evidence is equivocal, and clearly more studies, particularly prospective ones, are needed.
El-Sayed et al. [19]	Possible Association Between <i>Toxoplasma Gondii</i> Infection and	anti- <i>T. gondii</i> immunoglobulin G (IgG) antibody seropositivity and sICAM-1 serum level using commercially available enzyme-	The results showed that the seropositivity rate of anti- <i>T. gondii</i> IgG antibodies among schizophrenia patients (56.7%) was higher than	These statistically significant results support the association between <i>T. gondii</i> infection and schizophrenia and suggest the usefulness of sICAM-1 as

	Schizophrenia	linked immunosorbent assay kits.	among patients with depressive disorder (40%); despite this, the difference was not statistically significant. It was significantly higher in schizophrenia patients than in the healthy volunteers group (30%).	an indicator for the possible role of <i>Toxoplasma</i> among other factors in the etiopathogenesis of schizophrenia.
Rosado et al. [31]	Associations between <i>Toxoplasma gondii</i> seropositivity and psychopathological manifestations in schizophrenic patients: A single-center study from Ecuador	Study was conducted at the Neuroscience Institute of Guayaquil, Ecuador. Among 368 inpatients, 104 were selected based on specific inclusion and exclusion criteria. Descriptive statistics captured patient characteristics and mental health outcomes. Logistic regression models estimated the effect of toxoplasmosis on various mental health outcomes, controlling for demographic and health-related variables	86.5% of participants were seropositive for toxoplasmosis. <i>Toxoplasma</i> -seropositive schizophrenic patients had a lower risk of depression but a significantly higher risk of disorientation. The most prevalent mental health outcomes were Language Impairments (70.2%) and Bizarre Behavior (76.0%).	Findings suggest that <i>Toxoplasma gondii</i> seropositivity may have specific effects on mental functions in schizophrenic patients, particularly reducing the risk of depression but increasing the risk of disorientation. Further studies are required to clarify these associations and the potential underlying mechanisms.
Burgdorf et al. [32]	Large-scale study of <i>Toxoplasma</i> and Cytomegalovirus shows an association between infection and serious psychiatric disorders	This case-control study reviews register data on 81,912 individuals from the Danish Blood Donor Study to identify individuals who have a psychiatric diagnosis (N=2591), have attempted or committed suicide (N=655), or have had traffic accidents (N=2724). For all cases, controls were frequency matched by age and sex, resulting in 11,546 participants.	<i>T. gondii</i> was detected in 25.9% of the population and was associated with schizophrenia (odds ratio [OR], 1.47; 95% confidence interval [CI], 1.03–2.09). Accounting for temporality, with pathogen exposure preceding outcome, the association was even stronger (IRR, 2.78; 95% CI, 1.27–6.09). A very weak association between traffic accident and toxoplasmosis (OR, 1.11; 95% CI, 1.00–1.23, p = 0.054) was found.	This largest to date serological study provides evidence that exposure to <i>T. gondii</i> might be a contributing causal factor for developing schizophrenia and that exposure to CMV might be a contributing causal factor for developing serious psychiatric disorders. Research suggests that changes in dopamine levels are involved in the pathogenesis of toxoplasmosis-associated behavior changes in humans. These include prolongation of reaction time, decreased long-term concentration, decreased cognition and specific changes in neurodegenerative- and psychiatric disorders.

Khandaker et al. [16]	Prenatal maternal infection, neurodevelopment and adult schizophrenia: a systematic review of population-based studies	Electronic and manual searches, an objective assessment of individual-level prenatal maternal infection and standardized psychotic diagnoses in adult offspring. Methodological differences between studies necessitated a descriptive review.	Prenatal maternal non-specific bacterial, respiratory or genital and reproductive infection differed between studies, which reported up to a two- to fivefold increased risk of schizophrenia. Evidence for herpes simplex virus type 2 (HSV-2) and <i>Toxoplasma gondii</i> was mixed; some studies reported up to a doubling of schizophrenia risk. Prenatal HSV-1 or cytomegalovirus (CMV) infections were not associated with increased risk.	Prenatal exposure to a range of infections and inflammatory responses may be associated with risk of adult schizophrenia. Larger samples, mediation and animal models should be used to investigate whether there is a 'sensitive period' during development, and the effects of prenatal infections on neurodevelopment. Inclusion of genetic and immunological information should help to elucidate to what extent genetic vulnerability to schizophrenia may be explained by vulnerability to infection.
Mortensen et al. [10]	<i>Toxoplasma gondii</i> as a Risk Factor for Early-Onset Schizophrenia: Analysis of Filter Paper Blood Samples Obtained at Birth	This study was a cohort-based, case-control study combining data from national population registers and patient registers and a national neonatal screening biobank in Denmark. Patients included persons born in Denmark in 1981 or later followed up through 1999 with respect to inpatient or outpatient treatment for schizophrenia or related disorders (ICD-10 F2) or affective disorders (ICD-10 F3).	<i>Toxoplasma gondii</i> immunoglobulin G (IgG) levels corresponding to the upper quartile among control subjects were significantly associated with schizophrenia risk (odds ratio [OR] = 1.79, p = .045) after adjustment for urbanicity of place of birth, year of birth, gender, and psychiatric diagnoses among first-degree relatives. There was no significant association between any marker of infection and other schizophrenia-like disorders or affective disorders.	Study supports an association between <i>Toxoplasma gondii</i> and early-onset schizophrenia. Further studies are needed to establish if the association is causal and if it generalizes to cases with onset after age 18. The main finding of the study was a significant relationship between having an increased level of IgG antibodies to <i>T gondii</i> in newborn children and being diagnosed with schizophrenia prior to the age of 18. This study thus replicates the recent study reported by Brown et al (2005) of increased antibodies to <i>T gondii</i> in maternal sera from mothers who gave birth to children who later developed schizophrenia spectrum disorders.

DISCUSSION

Understanding the connection between *Toxoplasma gondii* and psychosis has become an important focus of research across psychiatry, neurology, immunology, and infectious disease. Although the exact ways the parasite relates to neuropsychiatric disorders are still being studied, a growing number of studies provide valuable insights into both the biological basis and the strength of this link. This section reviews key recent findings, looking at their methods, results, implications, and limitations. By comparing similarities and differences across studies, it aims to summarize current knowledge and point to directions for future research.

Liu et al. [9] conducted a large cross-sectional study in China, measuring anti-*Toxoplasma* IgM and IgG antibodies in psychiatric patients and the general population using ELISA. They found no significant difference in IgM positivity, but psychiatric patients showed higher IgG prevalence, indicating past infection. The study's large sample and broad diagnostic range are strengths, though its cross-sectional design limits conclusions about cause and effect. Fernandes et al. [27] performed a systematic review on exposure to neurotropic pathogens, including *T. gondii*, in newborns who later developed schizophrenia. After adjusting for many confounders, they found higher rates of *T. gondii* and cytomegalovirus antibodies in the schizophrenia group. Their longitudinal approach supports the idea that prenatal infection may affect later psychiatric health, but causality remains uncertain without genetic and immune data. Cossu et al. [28] carried out a meta-analysis of 23 studies with over 12,000 participants, where he found that people with bipolar disorder were more likely to test positive for *T. gondii* antibodies. This suggests the parasite's link to psychosis may extend beyond schizophrenia. However, differences in study quality and regional factors may have influenced these results. Campos-Carli et al. [29] reported different results in their ELISA study of chronic schizophrenia patients, finding no significant difference in *T. gondii* antibody rates between

patients and controls, nor links to clinical or cognitive outcomes. They suggested that strain differences or high infection rates in their sample might have hidden possible associations. This study highlights how population differences and confounding factors can affect findings. Ansari-Lari et al. [30] explored both the connection between *T. gondii* and schizophrenia and the parasite's link to suicidal behavior. They found a positive association with schizophrenia but observed fewer suicide attempts among seropositive males. These gender-specific results imply that latent infection may affect behavior differently in men and women, warranting further study. El-Sayed et al. [19] found higher *T. gondii* IgG positivity in schizophrenia patients compared to healthy controls, reinforcing the association. They also proposed soluble intercellular adhesion molecule-1 (sICAM-1) as a potential biomarker, offering a new angle for improving diagnosis or risk assessment. Rosado et al. [31] studied hospitalized schizophrenia patients in Ecuador and found an exceptionally high *T. gondii* infection rate (86.5%). Seropositivity was linked to more disorientation but less depression, suggesting the infection may differently affect cognitive and emotional symptoms. Burgdorf et al. [32] used data from over 81,000 individuals in Denmark in a large case-control study. They found *T. gondii* infection associated with schizophrenia, especially when infection occurred before psychiatric symptoms appeared. The study's size, use of national registries, and focus on timing strengthen the argument for a causal relationship. Khandaker et al. [16] reviewed population studies on prenatal infections, including *T. gondii*, and schizophrenia risk. They reported a two- to fivefold increased risk after maternal infection. Though evidence for *T. gondii* was mixed, their work supports the neurodevelopmental hypothesis and calls for future studies to include genetic and immune markers. Mortensen et al. [10] analyzed neonatal blood samples to study early *T. gondii* exposure and schizophrenia onset. They found higher IgG levels in individuals diagnosed before age 18. This influential study supports

the idea that prenatal or early postnatal exposure may increase vulnerability, backing early developmental models.

Together, these studies support the idea that exposure to *T. gondii*—especially early in life—may raise the risk of psychosis. However, results differ due to geographic, sample, strain, diagnostic, and methodological variations. The strongest evidence comes from large, longitudinal studies like those by Burgdorf et al. and Mortensen et al., which account for timing and confounding factors. Despite differences in methods, the overall pattern suggests *T. gondii* could act as an environmental trigger in genetically vulnerable individuals, affecting brain development, neurotransmission, and immune response. Future research should include genetic analysis, strain identification, and neuroimaging, and use standardized methods to clarify these links and explore treatment possibilities.

CONCLUSION

This study examined the link between *Toxoplasma gondii* infection and psychosis by looking at epidemiological data, theories about how it works, and evidence from both clinical and animal research. The results show a strong but complex connection, suggesting that *T. gondii* could be an environmental risk factor for developing or worsening psychotic disorders, especially schizophrenia. This connection seems to involve several biological pathways, including brain inflammation, dopamine imbalance, immune system activation, and genetic risk, and it may depend on when the infection occurs, such as during pregnancy or early childhood. Although the evidence is promising, proving a clear cause-and-effect relationship is still difficult. The research is wide-ranging but varies in sample types, diagnostic methods, and regional infection rates, making it hard to interpret and apply broadly. Still, the consistent findings across different studies highlight the need to consider infections in psychiatric research and treatment.

LIMITATIONS

Numerous constraints were identified throughout this assessment. A number of the studies analyzed were cross-sectional, restricting the capacity to deduce causality or temporal precedence. Also, the serological tests employed in many studies mainly indicate previous exposure instead of current infection, potentially undermining conclusions regarding the timing and significance of infection related to the onset of symptoms. Furthermore, the variability of *T. gondii* strains which could affect neuropathogenicity was not consistently considered, and only a few studies included genotyping of the parasite. Variables that could confound results, like socioeconomic status, geographic exposure risks, and co-infections, were not consistently managed in all studies. Moreover, there is a lack of extensive longitudinal and interventional studies that evaluate the effects of anti-parasitic or immunomodulatory therapies on psychiatric results. The variability in diagnostic criteria and psychiatric evaluations in different studies also represents a major drawback.

RECOMMENDATIONS

To enhance the understanding of the potential relationship between *Toxoplasma gondii* infection and psychosis, future research should adopt more rigorous and multidimensional approaches. Longitudinal studies are particularly important to establish the temporal sequence and potential causality between *T. gondii* exposure and the onset of psychotic disorders. Such studies would provide stronger evidence than cross-sectional designs and offer insights into the progression of psychiatric symptoms following infection. Standardization of diagnostic criteria and laboratory methodologies for both psychiatric conditions and *T. gondii* infection is essential. Harmonized tools would facilitate comparability across studies, enable meta-analytical synthesis, and strengthen the reliability of conclusions drawn from diverse populations. Incorporating host genetic profiling, immune system biomarkers, and cytokine analyses into future investigations

would help identify biological susceptibilities and clarify the mechanisms through which *T. gondii* may contribute to psychotic disorders. This integrative approach may reveal critical gene-environment interactions. Given the known variability in virulence and neurotropism among different strains of *T. gondii*, future studies should also include molecular strain typing. Identifying specific parasite genotypes associated with psychiatric outcomes could significantly advance understanding of differential pathogenic effects. Furthermore, interventional studies such as randomized clinical trials examining the efficacy of anti-parasitic or immunomodulatory treatments in seropositive individuals with psychosis could inform potential therapeutic strategies. These trials may help determine whether targeting latent infection has any effect on symptom severity or disease progression. Finally, public health initiatives should prioritize education on toxoplasmosis prevention, particularly among high-risk populations such as pregnant women and immunocompromised individuals. Enhanced awareness and preventive practices could contribute to reducing both the incidence of toxoplasmosis and its possible neuropsychiatric sequelae. By addressing these research and public health priorities, the scientific community can advance a more comprehensive understanding of *T. gondii*'s role in mental health, paving the way for evidence-based interventions and improved patient outcomes.

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