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Association Between Toxoplasma gondii Infection and Psychiatric Disorders: A Cross-Sectional Case–Control Study

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ABSTRACT

Toxoplasma gondii is an obligate intracellular parasite capable of establishing chronic infections in the central nervous system. Evidence suggests that chronic infection with this parasite may be associated with a broad spectrum of psychiatric disorders. This cross-sectional study investigated the association between T. gondii infection and depression, anxiety, and impulsivity. The study included 112 participants, comprising 45 individuals infected with T. gondii and 67 uninfected individuals, who were assessed using standardized questionnaires for depression, anxiety, and impulsivity. Toxoplasma infection was determined by serological testing using an enzyme-linked immunosorbent assay (ELISA). Data were analyzed using multivariate analysis of variance (MANOVA) and analysis of variance (ANOVA). The results demonstrated that scores for all psychological variables were significantly higher among individuals infected with T. gondii. The mean depression score was significantly higher in the infected group than in the uninfected group. Similarly, anxiety scores differed significantly between the groups. Impulsivity scores were also significantly higher in the infected group. Effect-size analysis (η^2) indicated small-to-moderate effects of infection on these variables, with η^2 values of 0.119 for depression, 0.122 for anxiety, and 0.087 for impulsivity. These findings highlight the importance of considering parasitic infections in psychiatric assessments and suggest screening for T. gondii infection in patients presenting with psychiatric symptoms, particularly in treatment-resistant cases.

Keywords: Toxoplasma gondii, depression, anxiety, impulsivity.

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Introduction

Toxoplasma gondii is an obligate intracellular protozoan parasite with a remarkably broad host range and a complex life cycle that enables persistent infection in humans and numerous warm-blooded animals. Human infection is highly prevalent worldwide and represents one of the most common parasitic infections of medical importance. Global seroepidemiological evidence indicates substantial geographic heterogeneity in exposure, reflecting differences in climate, dietary practices, sanitation, contact with cats, environmental contamination, and consumption of undercooked meat (1). Transmission commonly occurs through ingestion of tissue cysts in inadequately cooked meat or ingestion of oocysts contaminating food, water, or soil, and foodborne transmission remains an important route of human infection (2). Animal reservoirs also contribute to the maintenance of the parasite in the environment, and seroepidemiological investigations in

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livestock and wildlife have demonstrated the extensive ecological distribution of *T. gondii* across domestic and natural settings (3, 4). Although acute toxoplasmosis is frequently asymptomatic or mildly symptomatic in immunocompetent individuals, infection is generally followed by the establishment of latent tissue cysts, particularly within neural and muscular tissues, allowing the organism to persist for years or potentially for the lifetime of the host. The clinical significance of toxoplasmosis is well established in pregnancy, congenital infection, and immunocompromised patients, where severe neurological and systemic complications may occur (5). Increasingly, however, attention has shifted toward the possibility that chronic latent infection may also exert more subtle effects on the central nervous system, cognition, personality, emotional regulation, and psychiatric functioning.

The biological plausibility of a relationship between *T. gondii* and psychiatric outcomes is supported by the pronounced neurotropism of the organism. Following systemic dissemination, the parasite is capable of entering the central nervous system and establishing intracellular cysts in neurons and other neural cells. Rather than representing an entirely biologically inactive state, chronic infection may involve continuing interaction between parasite, neurons, glial cells, immune mediators, and neurotransmitter systems. Experimental work has shown that chronic *T. gondii* infection can inhibit neuronal function and alter neural signaling in animal models (6). Studies in adult mice have also demonstrated sensorimotor disturbances despite relatively preserved performance in some cognitive domains, suggesting that widespread neuropathology may produce selective rather than uniform behavioral consequences (7). Microglial activation is another potentially important mechanism. Primary cortical microglia demonstrate migratory activation in response to *T. gondii* infection, indicating that the parasite can initiate inflammatory and cellular responses within the brain (8). This is particularly relevant because microglia are now understood to participate not only in immune defense but also in synaptic remodeling, pruning, and regulation of neural circuitry (9). Persistent perturbation of these processes could theoretically influence the brain networks involved in mood regulation, behavioral inhibition, stress responsiveness, and cognitive control.

One of the most extensively investigated mechanisms linking *T. gondii* infection to behavioral change involves neurotransmitter metabolism. *T. gondii* has been shown experimentally to increase dopamine metabolism, providing a plausible neurochemical pathway through which infection could affect motivation, salience processing, impulsivity, reward-related behavior, and psychotic symptoms (10). The importance of dopaminergic signaling in major psychiatric disorders has long made this mechanism particularly noteworthy. In parallel, infection-induced immune activation may affect the kynurenine pathway, which is involved in tryptophan metabolism and produces neuroactive metabolites with potential effects on glutamatergic and dopaminergic neurotransmission. Experimental evaluation of kynurenine pathway metabolism in *T. gondii*-infected mice has raised important implications for neuropsychiatric disease, especially schizophrenia-spectrum pathology (11). These biochemical changes may interact with chronic neuroinflammation, oxidative stress, and altered neuron–glia communication, producing effects that are subtle at the individual level but potentially meaningful across large populations. The location of parasite cysts may also be relevant, because behavioral consequences may depend not merely on the presence of infection but on the specific neuroanatomical circuits affected (12). Such mechanistic evidence has contributed to the growing view that latent toxoplasmosis should not automatically be regarded as neurologically inert.

The strongest psychiatric literature concerning *T. gondii* has historically focused on schizophrenia and related psychotic disorders. Epidemiological and mechanistic findings have repeatedly suggested an association between toxoplasmosis and schizophrenia risk, although causality remains unresolved (13). Neuroimaging findings further support the possibility that infectious and inflammatory exposures could interact with structural and functional abnormalities already implicated in psychiatric disease. For example, schizophrenia has been associated with thalamocortical dysconnectivity, a systems-level disruption that may influence sensory integration, cognition, and behavioral regulation (14). Latent toxoplasmosis has also been associated with reductions in gray matter density among individuals with schizophrenia, suggesting that infection may interact with existing vulnerability rather than exert identical effects in all infected individuals (15). More broadly, altered prefrontal and fronto-amygdala connectivity has been implicated in severe psychiatric conditions characterized by affective and behavioral dysregulation (16). These neural systems overlap with those involved in anxiety, depression, impulsive behavior, and emotional control, which raises the possibility that the psychiatric relevance of *T. gondii* extends beyond psychotic disorders.

Evidence linking toxoplasmosis to cognition and behavior has indeed expanded beyond schizophrenia. Population-based research has identified associations between *T. gondii* infection and neurocognitive deficits, supporting the possibility that chronic infection may influence brain function even outside traditionally defined psychiatric populations (17). At the same time, population-representative cohort evidence has produced more cautious conclusions, with some studies finding limited or inconsistent relationships between seropositivity and broad measures of brain and behavioral impairment (18). These apparently divergent results underscore the complexity of the relationship and suggest that infection alone may be insufficient to determine psychiatric outcome. Host genetics, age at infection, parasite strain, immune status, cumulative infectious exposure, socioeconomic conditions, comorbid illness, and environmental stress may all moderate the behavioral consequences of toxoplasmosis. Recent reviews have therefore emphasized the need to understand the infection–behavior relationship as a host–parasite interaction rather than as a simple deterministic effect (19). Experimental studies of resistance to *T. gondii* infection further highlight the importance of immune mechanisms in determining host response, including pathways involving inducible nitric oxide synthase and other components of cellular defense (20).

Clinical observations have also supported a possible relationship between *T. gondii* and broader psychiatric phenotypes. Seropositivity has been reported more frequently among psychiatric patients diagnosed with personality disorders, suggesting that chronic infection may be associated with dimensions of behavior and personality rather than only categorical psychiatric diagnoses (21). Earlier work has similarly identified alterations in personality profiles among young women with latent toxoplasmosis (22). Cross-national ecological analyses have further linked latent toxoplasmosis with patterns of disease burden across countries, although such findings must be interpreted cautiously because ecological associations cannot establish individual-level causation (23). Nevertheless, these findings are consistent with the broader hypothesis that chronic infection could contribute to measurable differences in affect, personality, cognition, or behavior. The possibility that cumulative exposure to infectious agents may affect neuropsychiatric functioning has also been demonstrated in research examining combined Herpesviridae and *T. gondii* infections and their relationship with cognitive function among healthy individuals and patients with bipolar

disorder or schizophrenia (24). Such findings reinforce the need to consider infectious burden as one component within multifactorial models of psychiatric vulnerability.

Depression is particularly relevant in this context because it is among the most prevalent and disabling psychiatric conditions worldwide. Depression is heterogeneous in etiology and presentation, arising through complex interactions among biological, psychological, social, genetic, neuroendocrine, and inflammatory pathways. Epidemiological evidence consistently demonstrates sex differences in depression, with women generally exhibiting a higher prevalence than men (25). In Iran, depression represents an important mental health burden, and systematic evidence has documented considerable prevalence across patient populations (26). Infectious and inflammatory mechanisms have increasingly been investigated as possible contributors to depressive symptoms, particularly in cases characterized by atypical clinical trajectories or incomplete treatment response. Of specific relevance, prenatal research has found higher levels of depression and anxiety among women seropositive for *T. gondii*, supporting a potential association between infection and affective symptomatology (27). More recent case–control evidence has also identified an association between *T. gondii* seroprevalence and moderate or major depression in psychiatric patients, further strengthening interest in this relationship (28). Although such findings do not establish that infection directly causes depression, they suggest that serological status may constitute one biological factor associated with depressive symptom severity in selected populations.

Anxiety disorders are likewise highly prevalent and constitute a major source of disability and impaired quality of life. Their epidemiology demonstrates substantial variation across populations, but anxiety disorders collectively represent some of the most common mental disorders encountered in clinical practice (29). Large multinational studies have also confirmed the substantial burden of specific anxiety conditions such as social anxiety disorder across diverse countries and cultural contexts (30). Neurobiological models of anxiety implicate dysregulation within amygdala–prefrontal circuits, stress-response systems, neuroendocrine pathways, and genetic susceptibility (31). Because chronic toxoplasmosis may influence neuroinflammation, neurotransmission, and neural circuitry, there is biological justification for examining whether infection could be associated with heightened anxiety symptoms. The clinical importance of identifying additional biological correlates of anxiety is heightened by the fact that, although established interventions such as cognitive behavioral therapy are effective for many patients, response is not universal (32). Research using functional neuroimaging has shown that treatment-resistant psychiatric states may be characterized by distinct patterns of brain connectivity, suggesting that persistent symptoms can reflect biologically heterogeneous mechanisms (33). Thus, infectious exposures may be especially relevant to investigate in psychiatric presentations that do not conform fully to conventional psychosocial or neurobiological explanations.

Impulsivity represents another clinically important dimension because it cuts across numerous psychiatric conditions and is associated with impaired inhibition, rapid decision-making, reduced consideration of consequences, and difficulties in behavioral self-regulation. Although impulsivity is not a unitary construct, it generally encompasses attentional, motor, and non-planning components and is closely tied to frontostriatal and prefrontal control systems. Chronic alterations in dopamine metabolism caused by *T. gondii* provide one plausible pathway for altered impulsive behavior (10), while parasite-related disruption of neuronal function and immune–neural communication may provide additional mechanisms

(6, 8). Behavioral findings in infected animals and personality-related findings in humans have strengthened the hypothesis that latent toxoplasmosis may influence risk-taking or behavioral inhibition (7, 22). Nevertheless, impulsivity has received considerably less direct investigation than psychosis or cognition in the toxoplasmosis literature, leaving an important empirical gap.

Interpretation of the infection–psychiatric disorder relationship also requires caution because psychiatric illness itself may be associated with behavioral, socioeconomic, nutritional, or environmental factors that affect exposure to *T. gondii*. Reverse causation, residual confounding, and shared risk factors therefore remain plausible explanations for some reported associations. Moreover, *T. gondii* exposure may not operate in isolation but rather interact with pre-existing neurobiological vulnerabilities. Research in schizophrenia and bipolar disorder demonstrates that abnormalities in large-scale neural connectivity and prefrontal regulation are already present in many patients (14, 16), potentially creating a context in which infectious or inflammatory effects become more clinically salient. Likewise, some studies examining physiological abnormalities in recent-onset schizophrenia-spectrum disorders have emphasized the broader medical complexity of psychiatric populations and the need to integrate physical and mental health assessment (34). Such evidence supports a more integrated biopsychosocial model in which infectious disease, neural function, immune response, and psychiatric symptoms are evaluated together rather than treated as entirely separate domains.

From a clinical perspective, this issue has practical implications. If *T. gondii* seropositivity is associated with increased depression, anxiety, or impulsivity, screening for infection could potentially contribute to the characterization of selected psychiatric patients, particularly those with unusual symptom profiles, multiple risk factors, or resistance to standard treatment. This does not imply that serological testing should replace conventional psychiatric assessment or that infection is a primary cause of psychiatric illness. Rather, it suggests that latent infection may represent one of several biological variables capable of modifying psychiatric vulnerability. The historical focus on congenital and immunocompromised populations has understandably shaped the clinical understanding of toxoplasmosis (5), but accumulating evidence concerning cognition, personality, behavior, and psychiatric symptoms indicates that the potential neurological implications of chronic infection may be broader. Recent advances in understanding host behavior following infection have further strengthened interest in the parasite's capacity to influence neural and behavioral processes (19).

Despite this growing literature, important gaps remain. Many previous studies have concentrated on schizophrenia, cognitive impairment, personality characteristics, or narrowly defined populations, whereas simultaneous assessment of depression, anxiety, and impulsivity in relation to *T. gondii* serostatus remains comparatively limited. Furthermore, inconsistencies across studies suggest that replication in different populations is necessary. Some investigations support meaningful behavioral or neurocognitive associations (17, 23), whereas others indicate that the magnitude of these effects may be smaller or more context-dependent than initially proposed (18). These discrepancies make it particularly important to evaluate multiple psychological domains within the same analytic framework and to compare infected and uninfected individuals using standardized measures. Such an approach may help determine whether seropositivity is associated with a generalized pattern of psychological symptom elevation or whether associations are restricted to particular domains.

Accordingly, the aim of the present study was to investigate the association between *Toxoplasma gondii* infection and levels of depression, anxiety, and impulsivity by comparing seropositive and seronegative individuals.

Methods and Materials

Study Design and Participants

This study employed a case–control design. Participants were selected from volunteers who had been evaluated through a counseling and psychological services center. A total of 112 individuals, including 45 Toxoplasma-seropositive cases and 67 Toxoplasma-seronegative controls, were assessed for psychiatric symptoms using three standardized measures of anxiety, depression, and impulsivity.

Data Collection Tools

Blood samples were collected from the participants for serological detection of anti-*Toxoplasma* IgG antibodies.

Samples from both groups were analyzed for anti-*Toxoplasma* IgG antibodies using an enzyme-linked immunosorbent assay (ELISA) kit (Pishtaz Teb Company, Tehran, Iran).

The Beck Depression Inventory (BDI) is a 21-item self-report instrument widely used to assess the severity of depressive symptoms in both clinical and general populations. The inventory was originally introduced by Beck in 1961 (30) and revised in 1974 (31). It has demonstrated high reliability, validity, and concurrent validity. The instrument is practical to administer and requires approximately 5–10 minutes to complete.

The Barratt Impulsiveness Scale (BIS) was selected to assess impulsivity because a validated Persian version is available (32). This 30-item scale assesses three dimensions of impulsivity: attentional/cognitive impulsivity, motor impulsivity, and non-planning impulsivity. The scale, described by Barratt and colleagues (2008) within the framework of personality theory (33), has demonstrated strong correlations with established measures such as the Eysenck Personality Questionnaire. Its previous application in Iranian populations and intervention studies further supports its validity and suitability for the present study.

The Beck Anxiety Inventory (BAI) is a widely used 21-item self-report measure designed to assess the severity of clinical anxiety in adolescents and adults. Each item provides four response options reflecting increasing levels of symptom severity. The instrument has well-established validity and reliability. The BAI has also been validated in Iranian populations (34), supporting its suitability for both clinical and research applications in this context.

Data Analysis

The required sample size was calculated using G*Power software for multivariate analysis of variance (MANOVA) with three dependent variables (depression, anxiety, and impulsivity), two groups (infected and uninfected), $\alpha = 0.05$, and an effect size of $f^2 = 0.151$ ($\eta^2 = 0.05$). Data were analyzed using SPSS version 22. Descriptive statistics and inferential statistical procedures were applied, primarily multivariate analysis of variance (MANOVA), followed by appropriate post hoc analyses.

Findings and Results

Among the 112 participants, 45 (40.2%) were seropositive and 67 (59.8%) were seronegative for *Toxoplasma gondii*. In the *T. gondii*-seropositive group, 27 participants (60.0%) were women and 18 (40.0%) were men, whereas the seronegative group comprised 38 women (56.7%) and 29 men (43.3%). Regarding educational attainment, 20 seropositive participants (44.4%) had a bachelor's degree or higher-level university education, while 25 (55.6%) had a diploma or lower level of education. In the seronegative group, 35 participants (52.2%) had a bachelor's degree or higher-level education and 32 (47.8%) had a diploma or lower level of education. Thus, women constituted the majority of both groups, while lower educational attainment was somewhat more prevalent among *T. gondii*-seropositive participants.

Table 1. Descriptive Statistics for Depression, Anxiety, and Impulsivity According to *Toxoplasma gondii* Serostatus

Group	Variable	n	Mean	SD	Minimum	Maximum	Variance	Skewness	Kurtosis
T. gondii-seropositive	Depression	45	24.53	11.39	4	56	129.66	0.649	0.458
T. gondii-seropositive	Impulsivity	45	88.95	17.42	54	125	303.45	0.298	−0.444
T. gondii-seropositive	Anxiety	45	24.42	11.32	5	50	128.06	0.334	−1.027
T. gondii-seronegative	Depression	67	16.71	9.93	0	38	98.50	0.306	−0.911
T. gondii-seronegative	Impulsivity	67	81.00	11.24	53	104	126.34	0.035	−0.065
T. gondii-seronegative	Anxiety	67	16.56	9.77	0	38	95.43	0.251	−0.795

As shown in Table 1, participants who were seropositive for *T. gondii* obtained consistently higher mean scores on all three psychological measures than seronegative participants. The mean depression score was 24.53 (SD = 11.39) in the seropositive group compared with 16.71 (SD = 9.93) in the seronegative group. Similarly, the mean anxiety score was higher among seropositive participants (M = 24.42, SD = 11.32) than among seronegative participants (M = 16.56, SD = 9.77). Impulsivity scores followed the same pattern, with a mean of 88.95 (SD = 17.42) in the seropositive group and 81.00 (SD = 11.24) in the seronegative group. The seropositive group also displayed greater score variability, particularly for impulsivity. Skewness and kurtosis values were generally within acceptable ranges, indicating no substantial departure from univariate normality.

Before conducting the inferential analyses, the assumptions underlying multivariate analysis of variance (MANOVA) were examined. Because the data collection procedure required complete responses, no missing values were identified. Multivariate outliers were assessed using Mahalanobis distance, and no observation exceeded the critical chi-square threshold. Examination of skewness and kurtosis indicated approximately normal distributions for the dependent variables. Homogeneity of the variance–covariance matrices was supported by the nonsignificant Box's M test, Box's M = 11.416, $F(6, 60089.953) = 1.843$, $p = .087$. Levene's tests indicated homogeneity of variance for depression, $F(1, 110) = 0.76$, $p = .783$, and anxiety, $F(1, 110) = 3.179$, $p = .077$. The homogeneity assumption was violated for impulsivity, $F(1, 110) = 9.243$, $p = .003$. Nevertheless, the ratio of the larger impulsivity variance to the smaller variance was approximately 2.40:1 (303.45/126.34), remaining below the commonly accepted 4:1 threshold for substantial heteroscedasticity. Accordingly, the subsequent analyses were retained. MANOVA was then performed with depression, anxiety, and impulsivity as dependent variables and *T. gondii* serostatus as the independent variable. The overall multivariate effect of serostatus was statistically significant, Wilks' $\Lambda = .849$, $F(3, 108) = 6.40$, $p = .001$, $\eta^2 = .151$. Consistent results were obtained for Pillai's trace = .151, Hotelling's trace = .178, and Roy's largest

root = .178, indicating that the combined psychological profile differed significantly between *T. gondii*-seropositive and seronegative participants. The effect size indicated that approximately 15.1% of the multivariate variance in the combined dependent variables was associated with serostatus.

Table 2. Univariate ANOVA Results for Depression, Anxiety, and Impulsivity According to *Toxoplasma gondii* Serostatus

Variable	Mean Square	F	df	p	η^2
Depression	1644.90	14.823	1, 110	< .001	.119
Impulsivity	2066.50	10.480	1, 110	.002	.087
Anxiety	1661.00	15.311	1, 110	< .001	.122

Following the significant multivariate effect, univariate ANOVAs were conducted using a Bonferroni-adjusted significance level of $\alpha = .0167$. As presented in Table 2, statistically significant between-group differences were observed for all three dependent variables. Depression differed significantly according to *T. gondii* serostatus, $F(1, 110) = 14.823$, $p < .001$, $\eta^2 = .119$, indicating that approximately 11.9% of the variance in depression scores was associated with group membership. Anxiety also differed significantly between the groups, $F(1, 110) = 15.311$, $p < .001$, $\eta^2 = .122$, corresponding to an effect size of 12.2%. A significant difference was likewise found for impulsivity, $F(1, 110) = 10.480$, $p = .002$, $\eta^2 = .087$. Thus, the seropositive group demonstrated significantly higher depression, anxiety, and impulsivity scores than the seronegative group, and all three effects remained statistically significant after Bonferroni correction.

Table 3. Bonferroni-Adjusted Pairwise Comparisons Between *Toxoplasma gondii*-Seropositive and Seronegative Groups

Variable	Mean Difference (Seropositive – Seronegative)	SE	95% CI Lower	95% CI Upper	p
Depression	7.81	2.03	3.79	11.84	< .001
Impulsivity	8.76	2.71	3.39	14.13	.002
Anxiety	7.85	2.01	3.87	11.83	< .001

As shown in Table 3, Bonferroni-adjusted pairwise comparisons confirmed that *T. gondii*-seropositive participants had significantly higher scores on all three psychological outcomes. The mean depression score was 7.81 points higher in the seropositive group than in the seronegative group (SE = 2.03, 95% CI [3.79, 11.84], $p < .001$). Similarly, the seropositive group had an anxiety score that was, on average, 7.85 points higher than that of the seronegative group (SE = 2.01, 95% CI [3.87, 11.83], $p < .001$). The largest absolute mean difference was observed for impulsivity, for which seropositive participants scored 8.76 points higher than seronegative participants (SE = 2.71, 95% CI [3.39, 14.13], $p = .002$). Overall, the pairwise comparisons were consistent with the MANOVA and univariate ANOVA findings and demonstrated a systematic association between *T. gondii* seropositivity and higher levels of depression, anxiety, and impulsivity.

Discussion and Conclusion

The present study examined the association between *Toxoplasma gondii* infection and three psychological outcomes—depression, anxiety, and impulsivity—by comparing seropositive and seronegative individuals. The findings demonstrated a consistent pattern across all three domains. Participants who were seropositive for *T. gondii* had significantly higher scores for depression, anxiety, and impulsivity than seronegative participants. The multivariate analysis confirmed a statistically significant overall difference between the groups, with Wilks' $\Lambda = .849$, $F(3, 108) = 6.40$, $p = .001$, and $\eta^2 = .151$, indicating a moderate multivariate

effect. Subsequent univariate analyses showed significant effects for depression, $F(1, 110) = 14.823$, $p < .001$, $\eta^2 = .119$, anxiety, $F(1, 110) = 15.311$, $p < .001$, $\eta^2 = .122$, and impulsivity, $F(1, 110) = 10.480$, $p = .002$, $\eta^2 = .087$. Pairwise comparisons further showed that the seropositive group scored 7.81 points higher for depression, 7.85 points higher for anxiety, and 8.76 points higher for impulsivity. Taken together, these findings indicate that latent or chronic *T. gondii* infection was associated with a broader profile of increased psychological symptom burden rather than with a single isolated domain.

The finding concerning depression is consistent with an expanding body of evidence suggesting a relationship between *T. gondii* exposure and affective disturbances. The significantly higher depression scores observed among seropositive participants are particularly noteworthy given that depression is a multifactorial condition in which biological, inflammatory, neuroendocrine, and psychosocial factors interact. Previous research has identified an association between *T. gondii* seropositivity and depressive symptoms in several populations. For example, prenatal depression and anxiety were reported at elevated levels among women who were seropositive for *T. gondii*, suggesting that infection may be relevant to affective symptoms under conditions of physiological and psychological vulnerability (27). More recent case–control evidence has also shown increased *T. gondii* seroprevalence among psychiatric patients with moderate and major depression (28). These findings align with the present results and support the possibility that chronic infection may represent one biological correlate of depressive symptomatology. The magnitude of the effect observed in the present study, $\eta^2 = .119$, indicates that the association was not negligible and that serostatus accounted for a meaningful proportion of between-group variability in depression.

One possible explanation for the association between *T. gondii* infection and depression involves infection-related neuroinflammation and altered neuroimmune signaling. Chronic infection with *T. gondii* is characterized by persistent interaction between the parasite and the host immune system, including activation of glial cells in the central nervous system. Experimental evidence has shown that *T. gondii* can induce migratory activation of cortical microglia (8). Microglia are involved not only in immune defense but also in synaptic remodeling, neuronal homeostasis, and regulation of neural networks (9). Sustained microglial activation may therefore influence neural systems involved in mood regulation. Moreover, *T. gondii* infection may affect tryptophan and kynurenine metabolism, pathways increasingly implicated in psychiatric illness. Experimental work has demonstrated alterations in kynurenine pathway metabolism in infected animals, with potential consequences for glutamatergic and dopaminergic neurotransmission (11). These mechanisms provide a biologically plausible framework through which chronic infection could contribute to depressive symptoms, particularly in susceptible individuals.

The higher anxiety scores in the seropositive group similarly support a possible relationship between chronic toxoplasmosis and altered emotional regulation. Anxiety disorders are among the most prevalent psychiatric disorders internationally and are associated with dysregulation of neural systems involving the amygdala, prefrontal cortex, hypothalamic–pituitary–adrenal axis, and autonomic nervous system (29, 31). In the present study, anxiety exhibited the largest univariate effect size, $\eta^2 = .122$, suggesting that *T. gondii* seropositivity may be particularly relevant to anxiety-related symptom expression. The observed difference is consistent with prior evidence demonstrating elevated anxiety among *T. gondii*-positive women (27). It is also compatible with broader evidence indicating that chronic infectious and inflammatory processes can affect brain circuits involved in fear processing and emotional control. Functional dysconnectivity involving

prefrontal and limbic structures has been implicated in severe psychiatric disorders and may contribute to impaired regulation of affective responses (16). Although such findings do not directly establish that *T. gondii* causes anxiety, they provide a neural context within which infection-related changes could plausibly amplify anxious symptomatology.

Another explanation may involve the ability of *T. gondii* to affect neuronal function directly. In chronically infected mice, the parasite has been shown to inhibit neuronal activity (6). Experimental studies have also identified sensorimotor abnormalities in infected animals despite relatively preserved performance in some cognitive domains, suggesting that the consequences of infection may be selective and circuit-dependent (7). This selectivity is important when interpreting the present findings because anxiety may emerge from dysfunction within relatively specific neural systems even when global cognition remains intact. The location of parasite cysts and the neural circuits affected may therefore be central to understanding behavioral outcomes (12). Variability in cyst distribution could partly explain why some infected individuals remain psychologically asymptomatic whereas others show elevations in anxiety, depression, or behavioral dysregulation.

The significant association between *T. gondii* seropositivity and impulsivity is another important finding of this study. Compared with depression and anxiety, impulsivity has received less direct attention in toxoplasmosis research, yet there are strong mechanistic reasons to consider such a relationship. Impulsivity involves difficulties with inhibitory control, rapid responding, poor planning, and reduced consideration of future consequences, all of which depend heavily on prefrontal, frontostriatal, and dopaminergic systems. *T. gondii* has been shown experimentally to influence dopamine metabolism, which is particularly relevant because dopamine plays a central role in reward processing, motivation, risk taking, and behavioral control (10). The significantly higher impulsivity scores observed in the infected group are therefore consistent with the hypothesis that chronic infection may contribute to dysregulation within dopamine-dependent behavioral systems. Although the effect size for impulsivity was smaller than those observed for depression and anxiety, $\eta^2 = .087$, it still indicates a meaningful group difference.

Previous human studies also provide indirect support for this finding. Changes in personality profiles have been reported among individuals with latent toxoplasmosis, including differences in behavioral and personality characteristics that may overlap conceptually with impulsive tendencies (22). Seropositivity has also been reported more frequently in psychiatric patients diagnosed with personality disorders (21). These findings suggest that chronic infection may be associated not only with mood and anxiety symptoms but also with enduring or trait-like aspects of behavior. The broader literature on infection and behavior further supports this possibility, with reviews emphasizing that *T. gondii* may affect host behavior through complex interactions involving neurotransmitters, immune pathways, and neuroanatomical localization (19). The present findings extend this literature by demonstrating a measurable difference in impulsivity between infected and uninfected individuals using a standardized psychological instrument.

The combined elevation of depression, anxiety, and impulsivity observed in the infected group may indicate that the psychiatric relevance of toxoplasmosis is transdiagnostic rather than disorder-specific. Much of the earlier literature has focused on schizophrenia and psychosis, where associations with *T. gondii* have been repeatedly reported (13). Structural brain alterations have also been documented in seropositive patients with schizophrenia, including reduced gray matter density (15), while broader studies of

schizophrenia have identified disruptions in thalamocortical connectivity (14). These findings support the possibility that infection-related effects may interact with neural systems already implicated in psychiatric vulnerability. The present study suggests that similar processes may also be relevant to nonpsychotic dimensions such as depression, anxiety, and impulsivity. This is consistent with the notion that inflammatory and neurochemical disturbances can cut across conventional diagnostic categories and influence multiple forms of psychopathology.

At the same time, the present findings should not be interpreted as proof of a direct causal relationship between *T. gondii* infection and psychiatric symptoms. Some population-based research has found relatively modest or inconsistent associations between seropositivity and broad measures of brain and behavioral impairment (18). Other studies, however, have identified neurocognitive deficits associated with infection (17). These inconsistencies may reflect differences in study populations, age, socioeconomic status, parasite strain, timing of infection, immunological response, psychiatric comorbidity, and measurement methods. The consequences of *T. gondii* infection may also depend on cumulative biological burden and coexisting infectious exposures. For example, combined exposure to Herpesviridae and *T. gondii* has been associated with altered cognitive functioning in healthy individuals and patients with major psychiatric disorders (24). This supports a multifactorial model in which *T. gondii* may contribute to psychiatric vulnerability in interaction with other biological and environmental factors rather than functioning as an independent determinant.

The present results are also consistent with a broader ecological and epidemiological literature suggesting that toxoplasmosis may be associated with multiple dimensions of disease burden. Cross-national analyses have identified correlations between latent toxoplasmosis and disease patterns across populations (23), although such studies cannot determine causality at the individual level. The wide global distribution of the parasite (1) and its multiple routes of transmission, including foodborne exposure (2), make even relatively small psychiatric effects potentially important from a public health perspective. Animal reservoirs and environmental transmission contribute further to the ubiquity of exposure (3, 4). Therefore, clarification of whether latent infection contributes to psychiatric morbidity has relevance not only to psychiatry but also to infectious disease epidemiology and preventive medicine.

Host immune response may also help explain heterogeneity in psychological outcomes. Experimental research has shown that susceptibility and resistance to *T. gondii* infection depend partly on specific immune pathways, including inducible nitric oxide synthase-mediated mechanisms (20). Individual differences in immune regulation may therefore determine the extent to which infection affects neural tissue, inflammatory signaling, and behavioral function. In addition, developmental timing may be important. Congenital toxoplasmosis is well recognized as a condition with potentially serious neurological consequences, and long-term outcomes are strongly influenced by early diagnosis and treatment (5). Although the present study focused on adults and did not investigate congenital infection, this evidence illustrates the capacity of the parasite to produce persistent neurological effects and supports continued investigation of subtler outcomes associated with acquired or latent infection.

The clinical significance of the present findings lies in their demonstration of a consistent psychological profile associated with *T. gondii* seropositivity. The infected group showed higher levels of depressive symptoms, anxiety, and impulsivity, and these differences remained significant after adjustment for multiple

comparisons. Such findings may be especially relevant in cases in which symptoms are persistent or resistant to conventional treatment. Evidence from psychiatric neuroscience indicates that treatment-resistant conditions can differ biologically from treatment-responsive forms, including differences in brain connectivity (33). Established psychotherapeutic interventions such as cognitive behavioral therapy are effective across many psychiatric conditions (32), but not all patients respond adequately. Although serological screening cannot currently be considered a routine psychiatric diagnostic procedure, the present results support further investigation into whether infectious status may help explain symptom heterogeneity in selected patients.

The findings should also be interpreted within the broader epidemiology of depression and anxiety. Depression is more prevalent among women in many populations (25), and anxiety disorders similarly show substantial demographic and geographic variation (30). In Iran, depression represents an important clinical burden (26). Such background prevalence means that observed psychiatric symptoms cannot be attributed to infection alone. Nonetheless, the significant differences between seropositive and seronegative participants in this study suggest that *T. gondii* infection may be one contributory factor among many. The presence of medical and physiological abnormalities in psychiatric populations more generally further supports the need for integrated models that do not artificially separate mental and physical health (34). In this context, toxoplasmosis may represent one example of how chronic biological exposures intersect with psychiatric symptom expression.

This study has several limitations that should be considered when interpreting the findings. First, the case–control and cross-sectional nature of the design prevents determination of temporal sequence or causality, and it therefore cannot be concluded that *T. gondii* infection directly caused the higher levels of depression, anxiety, or impulsivity observed in the seropositive group. Second, the sample size was relatively modest and participants were recruited from a limited setting, which may reduce generalizability to broader clinical and community populations. Third, the psychological variables were assessed using self-report questionnaires, which may be influenced by response bias, current mood, or social desirability. Fourth, serological assessment of IgG antibodies indicates previous exposure but does not establish the timing, duration, parasite strain, cyst burden, or current biological activity of infection. Finally, potentially important confounding variables such as socioeconomic status, dietary habits, contact with cats, medication use, substance use, comorbid medical conditions, inflammatory markers, and other infectious exposures were not comprehensively controlled.

Future research should employ larger, multicenter, and longitudinal designs to clarify the temporal relationship between *T. gondii* infection and psychiatric symptoms and to determine whether infection predicts changes in depression, anxiety, or impulsivity over time. Studies should also incorporate more detailed serological and molecular measures, including IgG titers, IgM status where appropriate, avidity testing, inflammatory biomarkers, and, when feasible, characterization of parasite strains. Neuroimaging, neurocognitive testing, and assessment of dopaminergic and kynurenine-related pathways could help clarify the mechanisms underlying the observed associations. Future investigations should also examine potential moderators such as sex, age, immune status, socioeconomic conditions, genotype, treatment exposure, and duration of infection. Prospective studies of treatment-resistant psychiatric populations may be particularly valuable in determining whether *T. gondii* status identifies a clinically meaningful subgroup.

From a practical perspective, clinicians should remain aware that psychiatric symptoms can coexist with chronic infectious and inflammatory conditions and should consider a broader medical evaluation when symptoms are atypical, severe, persistent, or resistant to standard interventions. Screening for *T. gondii* infection may be considered in selected high-risk patients rather than as a universal psychiatric test, particularly when there is a relevant exposure history or other clinical indication. Collaboration between psychiatrists, psychologists, infectious disease specialists, and primary care physicians may improve recognition of biological contributors to psychiatric symptoms. Preventive education concerning safe food preparation, avoidance of undercooked meat, hand hygiene, and appropriate management of exposure to potentially contaminated soil or cat feces may also be beneficial as part of broader toxoplasmosis prevention strategies.

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Authors' Contributions

All authors equally contributed to this study.

Declaration of Interest

The authors of this article declared no conflict of interest.

Ethical Considerations

The study protocol adhered to the principles outlined in the Helsinki Declaration, which provides guidelines for ethical research involving human participants.

Transparency of Data

In accordance with the principles of transparency and open research, we declare that all data and materials used in this study are available upon request.

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