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Toxoplasma Infection

Ashkan Latifi and Jaroslav Flegr
Department of Philosophy and History of Science, Faculty of Science, Charles University, Prague, Czech Republic

Synonyms

Chronic toxoplasmosis; Latent toxoplasmosis; *Toxoplasma gondii*; Toxoplasmosis

Definition

Toxoplasmosis, a disease caused by the microscopic parasite *Toxoplasma gondii*, can manifest in four forms – congenital, acute, chronic, and latent. Latent toxoplasmosis, the most common form affecting about 30% of the global human population as well as various animal species, can influence behavior, cognition, and personality.

Introduction

Toxoplasma gondii, an obligate intracellular protozoan, has the capacity to infect almost all warm-blooded vertebrates. It is believed that about a third of the global human population is infected with this parasite. Cats, the definitive hosts of *Toxoplasma*, provide an environment for the parasite's sexual reproduction, which results in the production of oocytes. Following excretion in feline feces, a sporulation process over a period of 2–5 days converts these oocytes into infectious agents. When these agents are ingested by an intermediate host, zoites inside the oocysts undergo transformation into tachyzoites, which invade the host cells, where they quickly multiply asexually and disseminate throughout the host's body.

If a woman contracts the infection during pregnancy, there's a risk that the embryo may also become infected. This could lead to the development of congenital toxoplasmosis, which is the most severe form of the disease. The potential outcomes are miscarriage, fetal defects, and a variety of complications in newborns, including encephalitis, cerebral calcification, chorioretinitis, hydrocephalus, microcephaly, mental retardation, deafness, and blindness (see Johnson & Johnson, 2021; Tong et al., 2021).

In the event of postnatal *Toxoplasma gondii* infection, an acute stage ensues, characterized by rapid tachyzoite multiplication and symptoms akin to common viral illnesses, like influenza. This stage persists for several weeks. In immunocompetent hosts, this phase spontaneously transitions into a latent stage, during which tissue cysts form to house dormant bradyzoites. Predominantly located in immunoprivileged organs such as the central nervous system and brain, eyes, and testes, these cysts can persist in the host's tissues for a lifetime and are capable of infecting a new host upon ingestion. Rarely, and likely only in

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individuals with certain immune disorders, some pathological symptoms of acute toxoplasmosis may persist or recur months and years later. In such cases, we refer to this condition as chronic toxoplasmosis.

Toxoplasma can be transmitted through a variety of pathways. These include ingestion of vegetables contaminated with oocysts, consumption of undercooked meat containing tissue cysts, blood transfusions, organ transplants, or potentially sexual intercourse (see Johnson & Johnson, 2021; Tong et al., 2021).

Latent toxoplasmosis doesn't exhibit distinct signs or symptoms. While historically considered harmless in immunocompetent individuals, recent research conducted over the past three decades has highlighted its impact on infected individuals' personality, behavior, mental health, and cognition. Studies from the 1980s reported behavioral changes in infected mice, including impaired motor performance and increased mobility. During the 1990s, human studies noted alterations in the personality profiles of infected individuals. Subsequently, links between toxoplasmosis and mental disorders, particularly schizophrenia, as well as cognitive deficits, were identified.

During the same decade, an evolutionary explanation for these changes was proposed, grounded in the manipulation hypothesis (Barnard & Behnke, 2005). It suggested that these behavioral shifts in hosts were not coincidental, but deliberate manipulations by the parasite to facilitate its transmission. The evidence for this hypothesis was particularly suggestive in rodents, where behavioral changes induced by infection increased their susceptibility to predation, thus enhancing parasite transmission. The specifics of these manipulations and the mechanisms involved will be further explored in this article.

Toxoplasma gondii, Personality, Behavior, and Cognition

Toxoplasma gondii and Personality

Long-term *Toxoplasma* infection, or latent toxoplasmosis, has been linked to shifts in human personality traits. A comprehensive review of studies spanning two decades concluded that the personality profiles of infected subjects were significantly distinct from those of uninfected individuals. The studies primarily employed tools such as Cattell's 16PF, Cloninger's TCI, and the Big Five Personality Inventory (Flegr, 2013). Flegr's review acknowledged the critical role of sex in these personality shifts, to the point that some changes were diametrically opposite in infected men and women. The review additionally noted that several studies identified a direct relationship between the duration of infection and these personality shifts. This implies that as the length of infection increased in subjects (or as the anti-*Toxoplasma* antibody titers decreased), the corresponding personality changes became more pronounced. According to this review, toxoplasmosis generally resulted in a decrease in the novelty seeking in both infected men and women (measured by Cloninger's TCI), while infected men exhibited increased extraversion and decreased conscientiousness (measured by NEO-PI-R). Furthermore, infected women were found to be more outgoing, relaxed, and warm-hearted than uninfected women, while infected men were more jealous, suspicious, and dismissive of rules compared to their uninfected counterparts (as measured by Cattell's 16PF).

Toxoplasma gondii and Behavior

As previously mentioned, behavioral changes in animals infected with *Toxoplasma* were noted by researchers as far back as the 1980s. Studies on infected humans have similarly uncovered the capability of *Toxoplasma* to induce behavioral changes.

A study, based on the psychological perspective that men and women employ different strategies in stressful situations (with men typically using problem-focused coping strategies and withdrawal, while women tend to express their emotions and prefer social integration), implemented the method of experimental games, specifically the Trust Game and a modified Dictator Game (Lindová et al., 2010). Aligning with the stress coping hypothesis, infected men displayed non-cooperative behavior in all scenarios, while infected women were non-cooperative solely in the Dictator Game. Notably, in the Trust Game, where interpersonal context is crucial, infected

women demonstrated greater cooperativeness than their non-infected counterparts.

Another study investigated the impact of toxoplasmosis on entrepreneurship activity (Johnson et al., 2018). It showed that *Toxoplasma*-infected subjects were 1.4 times more likely to study business and 1.7 times more likely to focus on "management and entrepreneurship" than their uninfected counterparts. Also, infected subjects were 1.8 times more likely to have started a business. At the societal level, *Toxoplasma* infection was a reliable predictor of entrepreneurial activity at the national level, regardless of other economic covariates in the models. Hence, nations with a higher prevalence of toxoplasmosis had higher levels of entrepreneurial activity. The study further revealed a positive association between a higher prevalence of *Toxoplasma* infection in a country and a lower rate of "fear of failure" when starting a new business.

A systematic review of studies published since 1990 on the effects of toxoplasmosis on human behaviour highlighted that infected subjects, men but not women, struggled more to form personal relationships, demonstrated reduced self-control, and were more likely to wear unkempt clothes (Martinez et al., 2018). In addition, this review reported that infected male subjects were more impulsive, and infected females demonstrated higher trait reactive aggression than the controls.

Another review pointed to a phenomenon seen in infected rodents, the attraction to predator odor, which is evident in both *Toxoplasma*-infected chimpanzees and humans as well (Johnson & Johnson, 2021). As the review pointed out, infected chimpanzees were attracted to the urine of leopards, their only natural predators, but not to other felines' urine. Interestingly, infected men rated the smell of cat urine as more pleasant compared to uninfected male controls, whereas infected women found it less pleasant than uninfected female controls. Additionally, the review referenced a study where subjects infected with *Toxoplasma* appeared to be less swayed by monetary incentives, implying that the infection might modify the "risk versus reward" balance in these individuals.

Toxoplasma Gondii and Cognition

Research suggests a link between *Toxoplasma* infection and alterations in cognitive functions. A systematic review and meta-analysis explored this association (de Haan et al., 2021). The review included only studies that tested healthy subjects for anti-*Toxoplasma* antibodies and evaluated their cognitive functions using neuropsychological tests. In total, it analyzed 13 studies involving 13,289 participants, where the means and standard deviations of cognitive scores were provided. The meta-analysis examined outcomes in four cognitive domains. Considering processing speed, evaluated by tests such as the Trail Making Test Part A, the Serial Reaction Time Test, or the go/no-go reaction time test, a small but statistically significant positive association was found between *Toxoplasma* infection and this cognitive domain.

With regards to working memory, evaluated by tests like the Wechsler Adult Intelligence Scale or the Wechsler Intelligence Scale for Children Digit Span test, a small but statistically significant association between toxoplasmosis and impaired working memory function was observed.

In terms of short-term verbal memory, assessed by tests such as the Auditory Verbal Learning Test, the California Verbal Learning Test, or the Verbal Learning and Memory Test, a statistically significant association between *Toxoplasma* infection and verbal memory impairment was found.

Finally, regarding executive functions, measured by the Trail Making Test Part B, verbal fluency tests, or clock drawing tests, a statistically significant association between *Toxoplasma* infection and impaired executive functioning was detected.

In summary, this meta-analysis found that *Toxoplasma*-seropositivity was associated with impaired cognitive function in infected subjects.

Toxoplasma has also been associated with changes in intelligence. From an evolutionary standpoint, one might hypothesize that reducing a host's intelligence, potentially through manipulation of the dopaminergic pathway, could benefit *Toxoplasma* by making the infected host more susceptible to predation. In support of this notion,

several human studies have found a negative correlation between *Toxoplasma* infection and verbal intelligence scores, with infected individuals scoring lower than their uninfected counterparts (Flegr et al., 2003, but also see Flegr et al., 2023).

Certain studies have also suggested that the effects of toxoplasmosis on intelligence may vary depending on an individual's Rh factor status (Flegr et al., 2013). In an investigation involving 502 soldiers and utilizing two intelligence tests (the Wiener Matrizen-Test for nonverbal intelligence and the OTIS test for verbal intelligence), researchers found an interaction between subjects' Rh phenotype and their *Toxoplasma* infection status with respect to intelligence scores.

The initial analysis did not identify a correlation between toxoplasmosis and either nonverbal or verbal intelligence within the RhD unsorted population. However, further analysis considering the RhD status of the subjects showed that Rh-positive infected individuals had lower verbal and nonverbal intelligence scores compared to Rh-positive uninfected subjects. On the contrary, Rh-negative subjects exhibited the opposite: Rh-negative infected individuals had higher verbal and nonverbal intelligence scores than Rh-negative uninfected participants.

These observations suggest a significant role of the RhD phenotype in human physiology. While the study did not propose a clear explanation for the observed effects on intelligence, it suggested that the RhD gene, other genes linked to it, or other confounding variables might be involved (Flegr et al., 2013). Regardless, based on these findings, it is evident that the interaction between RhD phenotype and toxoplasmosis explains a portion of the variance in the observed effects of toxoplasmosis on human intelligence.

Toxoplasma gondii and Sexual Behavior

Research into the influence of toxoplasmosis on sexual behavior follows three primary directions. The first primary line of research focuses on the impact of infection on the behavior of uninfected individuals toward those who are infected. For many species, the infection is transmitted from male to female through semen during sexual intercourse. If *Toxoplasma* could enhance the sexual attractiveness of infected males to uninfected females, it would thereby increase the efficiency of its sexual transmission.

The second line of research examines the impact of toxoplasmosis on the behavior of infected individuals. Specifically, changes in sexual behavior, such as heightened promiscuity or increased frequency of sexual intercourse among infected individuals, could potentially enhance the efficiency of transmission from infected to uninfected individuals, thereby facilitating the spread of the infection.

The third direction of research considers the potential for *Toxoplasma* to enhance its transmission efficiency via the alimentary route, specifically through predation, by inducing changes in sexual behavior. Investigations into the "fatal attraction" phenomenon (see Berdoy et al., 2000) suggest that infected intermediate hosts may be lured by the scent of the definitive host. This allure is likely caused by epigenetic changes in the brain of infected individuals, where stimuli typically inducing fear in uninfected counterparts instead stimulate sexual arousal in those infected.

The Influence of Toxoplasmosis on Non-infected Individuals' Behavior Toward Infected Individuals

A pivotal component of studying toxoplasmosis' impact on sexual behavior is analyzing the response of uninfected animals or humans toward their infected sexual partners. It has been observed that females across many species typically avoid male counterparts burdened with parasites. They do so for two key reasons – firstly, to ensure their offspring do not inherit genes predisposing them to such parasites (*good genes hypothesis*), and secondly, to evade the risk of contracting the infection itself from infected males. This latter point is especially relevant if the parasite has the potential for sexual transmission (*good parents hypothesis*), which seems likely in the case of *Toxoplasma*. In sexually transmitted parasites, individuals of the host species are under selective pressure to avoid reproducing with infected individuals. Conversely, the parasite is subject to

selective pressure to manipulate uninfected members of the host species to preferentially reproduce with infected members of the host species. This can primarily be achieved by enhancing the sexual attractiveness of infected individuals, especially infected males. Predicting which of these selective pressures will prevail in a specific parasite-host pairing is not feasible in advance, as both possibilities could potentially occur.

The Evidence for Sexual Transmission of Toxoplasmosis

The potential for the sexual transmission of *Toxoplasma* has been demonstrated in various host species, for recent review see (Hlaváčová et al., 2021). However, this same study also introduced new evidence for the existence of sexual transmission of toxoplasmosis in humans. The authors administered a series of questionnaires to a large sample of couples. These questionnaires sought to collect data on various aspects, including the couples' medical history, age, relationship status, epidemiological risk factors, history of unprotected sexual intercourse, pet ownership (specifically cats), consumption of poorly washed fruits and vegetables, unprotected exposure to garden soil, and residential history during their childhood years. All individuals in the couples were also tested for toxoplasmosis. The findings from this research showed a marked difference in toxoplasmosis prevalence between women who had toxoplasmosis-infected male partners and those with uninfected male partners. The data indicated that women with infected partners were significantly more likely to contract the parasite.

Notably, the prevalence of toxoplasmosis showed no significant difference between men who had infected female partners and those with uninfected female partners. Based on these findings, Hlaváčová et al. propose that the sexual transmission of toxoplasmosis in humans appears to be predominantly unidirectional, occurring primarily from infected men to women. Furthermore, this mode of transmission does not appear to be influenced by shared risk factors between partners.

Effect of Toxoplasmosis on the Sexual Attractiveness *Toxoplasma*-Infected Rats

An animal model study was conducted in male rats to investigate the impact of toxoplasmosis on the sexual behavior of uninfected females. The study found no significant difference between *Toxoplasma*-infected male rats and their uninfected counterparts in terms of sexual behavior or fecundity/fertility (Hari Dass et al., 2011). This included factors such as the number of offspring, the weight of newborns, the sex ratio of the offspring, and the frequency of mounting and intromission during mating with uninfected females. However, the study observed that uninfected females consistently and significantly preferred infected males over uninfected ones in a two-choice preference task. Infected males also secured a larger number of reproductive opportunities than uninfected males in a competitive paced mating scenario. These findings suggest that *Toxoplasma* may strategically manipulate the sexual attractiveness of infected males to uninfected females. As a result, the altered sexual behavior in females leads to increased opportunities for the parasite to be transmitted from males to females via sexual contact.

Effect of Toxoplasmosis on the Sexual Attractiveness *Toxoplasma*-Infected Men

Evidence suggests that *Toxoplasma* can enhance the sexual attractiveness of infected individuals, thereby increasing its chances of sexual transmission, even in humans. For example, a study that investigated morphological differences between *Toxoplasma*-infected and uninfected university students ($n = 268$) found that infected male subjects were significantly taller than the uninfected males. However, no such difference was detected between infected and uninfected female subjects (Flegr et al., 2005). Another study demonstrated that when 109 female students were shown facial images of 89 male students (18 of whom were *Toxoplasma*-infected), the results, after adjusting for age, indicated that *Toxoplasma*-infected subjects were perceived as more dominant ($p < 0.01$) and masculine ($p = 0.052$) (Hodková et al., 2007). The study also revealed that infected men had a lower 2D:4D ratio, a marker of higher

prenatal (and possibly also postnatal) concentration of testosterone. However, the results for perceived dominance and masculinity remained consistent even after controlling for 2D:4D ratios, suggesting that these two characteristics were independent.

In a more recent study, researchers examined a variety of factors, including the number of minor health issues, self-perceived attractiveness, facial width-to-height ratio, handgrip strength, number of sexual partners, body mass index, mate value, and facial fluctuating asymmetry, in a sample of 35 *Toxoplasma*-infected and 178 uninfected subjects (Borráz-León et al., 2022). The subjects were required to self-report data related to the aforementioned factors via several questionnaires. Additionally, a group of independent evaluators (146 women and 59 men) assessed the perceived health and attractiveness of facial pictures of both *Toxoplasma*-infected and uninfected subjects. The results indicated that the infected men and women were rated as more attractive than the uninfected controls. In particular, infected men were found to have lower facial fluctuating asymmetry. Moreover, infected women were also found to have a tendency toward lower facial fluctuating asymmetry, lower body mass index, a higher number of sexual partners, and higher self-perceived attractiveness. According to Borráz-León et al., these observations could be a direct effect of *Toxoplasma* infection or they could be the result of highly symmetrical subjects effectively managing the physiological costs of parasitism. The researchers maintained that findings from both animal models and human studies leaned toward the former possibility, but empirical confirmation is still needed.

Nonetheless, as already discussed, based on the independence of 2D:4D ratios from perceived dominance and masculinity, it can be suggested that postnatal upregulation of testosterone synthesis is likely an effect induced by *Toxoplasma* infection. In conclusion, evidence from both human and animal models suggests that *Toxoplasma* can potentially alter certain physical characteristics that increase the attractiveness of infected males to females. This appears to be an example of parasite-induced manipulation.

Impacts of Toxoplasmosis on the Sexual Behavior of Infected Individuals

The effects of *Toxoplasma* infection on the intermediate host's sexual behavior have been examined in both animal and human studies. As mentioned above, there were no significant differences in the sexual behavior of infected and uninfected male rats. However, as predicted by the manipulation hypothesis, Toxoplasma is expected to be able to manipulate the sexual behavior of infected animals to enhance its probability of transmission from the infected intermediate host to the definitive host, a feline, through predation.

Many studies reported a significant difference in the behavioral response to predator presence between rats infected with *Toxoplasma* and uninfected rats. More particularly, the evolved innate aversion to cat odor was altered in the infected animals. Observation of the rats' nocturnal exploratory behavior showed that infected rats more frequently approached corners of their enclosures containing cat odor compared to corners with other scents, such as their own smell, a neutral scent, or rabbit odor. This was referred to as the "fatal attraction phenomenon" by the researchers (Berdoy et al., 2000).

Another study (House et al., 2011) indicated that this phenomenon was induced by *Toxoplasma* infection through an epigenetic manipulation of the medial amygdala in the infected host. Two anatomically contiguous pathways, the defensive and reproductive pathways, were affected in a way that the activity of the defensive pathway, which typically elicits flight in response to predator-related stimuli (e.g., cat urine odor), was disturbed and intermingled with activity in the reproductive pathway. This was suggested to lead to the observed fatal sexual attraction of the infected host to the scent of cat urine.

Only one published study has delved into the effects of toxoplasmosis on human sexual behavior (Flegr & Kuba, 2016). This study utilized a sample comprising of 5,087 *Toxoplasma*-free and 741 *Toxoplasma*-infected individuals who responded to a series of five questionnaires aimed at assessing sexual narcissism, sociosexual orientation, disgust sensitivity, dominance, and attraction to sexual aggression.

Despite being less engaged in activities like getting tattoos and piercings, watching pornography, participating in group sex, and in practices associated with Bondage, Discipline, and Sado-Masochism (BDSM), individuals infected with *Toxoplasma* reported a heightened interest and arousal toward these activities. The study also revealed that infected individuals reported higher attraction to fetishism, zoophilia, bondage, violence, and for infected males, toward acts of rape, being raped, and masochism. This dichotomy between fantasy and actual practice suggests that while infected individuals reported higher levels of interest in such activities, they were less likely to actualize them than their uninfected counterparts, possibly due to the energy-consuming toll of latent toxoplasmosis.

The reasons for the prevalence of such fantasies in *Toxoplasma*-infected individuals remain unclear. However, it is hypothesized that the engagement in these less conventional sexual activities could potentially contribute to the sexual transmission of toxoplasmosis. Furthermore, the affinity for masochism might be seen as a non-adaptive manifestation of the "fatal attraction" phenomenon within the human species, specifically as a result of the association between fear and sexual arousal in infected individuals, also refer to the chapter Postadaptations.

Toxoplasma gondii and Mental Disorder

The relationship between *Toxoplasma* infection and mental disorders has been emphasized in numerous studies, and evidence supporting this link has grown significantly over the past few decades. Specifically, the correlation between toxoplasmosis and schizophrenia has been investigated for at least 50 years. Older meta-analytical studies show that latent toxoplasmosis nearly triples the risk of developing schizophrenia (odds ratio= 2.73; 95% CI 2.10–3.60) (Torrey et al., 2012).

A recent review of research in this area suggests that infectious agents, including *Toxoplasma*, may induce a variety of psychiatric disorders (Maisarah et al., 2022). The review proposes that this could be a result of the host's immune response, which can either directly or indirectly affect the central nervous system (CNS). This review, based on the findings of a meta-analysis, concludes that there may be a correlation between obsessive-compulsive disorder (OCD) and toxoplasmosis infection, with a notable common odds ratio of 1.96 reported in the original study. The review also investigates the link between toxoplasmosis and Alzheimer's disease (AD), citing a meta-analysis. The original study identified *Toxoplasma* infection as a risk factor for developing AD or exacerbating its symptoms, with a significant odds ratio of 1.53.

The review also notes that, based on another meta-analysis, toxoplasmosis appears to contribute significantly to traffic accidents and suicide attempts, with statistically significant odds ratios reported in the original meta-analysis (odds ratio = 1.39 for suicide attempts; odds ratio = 1.69 for traffic accidents). Considering the topic of Attention-Deficit Hyperactivity Disorder (ADHD), the review cites a systematic review and meta-analysis that reports a non-significant association between *Toxoplasma* infection and ADHD, with an odds ratio of 2.02. However, both the review and the original study argue that it's unclear whether or not toxoplasmosis is a risk factor for developing ADHD due to the limited number of studies on this correlation. Regarding autism, the review notes that the original study reported an association between latent toxoplasmosis and Autism Spectrum Disorders (ASD), with an odds ratio of 1.93 (95% CI 1.01–3.66). It is noteworthy that, the original study reported no association between acute toxoplasmosis and ASD. In conclusion, these meta-analyses suggest that toxoplasmosis can be considered as a risk factor for the development of OCD, AD, ASD, and possibly ADHD.

Another meta-analysis of 50 studies investigating the relationship between *Toxoplasma* infection and mental disorders included a total of 12,009 cases and 71,441 healthy controls (Sutterland et al., 2015). The study reported an overall significant odds ratio of 1.81 (95% CI 1.51–2.16, $P < 0.00001$) between schizophrenia and *Toxoplasma* infection. The meta-analysis

highlighted the "toxoplasmosis disease phase" as an important factor in this relationship, revealing an association of increased risk of toxoplasmosis prior to the onset of schizophrenia (odds ratio = 1.30, 95% CI 1.05–1.61, $P = 0.017$). The study also found substantial odds ratios for toxoplasmosis and recent onset schizophrenia (odds ratio = 2.18, 95% CI 1.58–3.01, $P < 0.00001$) as well as toxoplasmosis and chronic schizophrenia (odds ratio = 1.88, 95% CI 1.46–2.42, $P < 0.000001$). No significant effect of sex on the odds ratio was observed ($p = 0.90$).

Regarding bipolar disorder, the meta-analysis found a significant odds ratio of 1.52 (95% CI 1.06–2.18, $P = 0.02$), indicating an association between *Toxoplasma* infection and the disease. The same study also analyzed the association between toxoplasmosis and major depression, yielding a non-significant overall odds ratio of 1.21 (95% CI 0.86–1.70, $P = 0.28$). In terms of obsessive-compulsive disorder (OCD), the overall odds ratio was 3.4 (95% CI 1.73–6.68, $P = 0.0004$), suggesting a strong relationship between *Toxoplasma* infection and OCD development. Finally, the study found a significant odds ratio of 1.91 (95% CI 1.49–2.44, $P < 0.00001$), indicating a higher prevalence of *Toxoplasma* infection in heroin addicts. However, the number of studies analyzed was low for this category. In summary, the results of this meta-analysis suggest that toxoplasmosis can be a risk factor for schizophrenia, OCD, bipolar disorder, and addiction, but not for depression.

Toxoplasma gondii and Behavioral Changes: A Consequence of Health Deterioration from Infection?

The most straightforward explanation for behavioral changes associated with infection by any pathogen is that these alterations are due to the compromised health of infected individuals. For many years, latent toxoplasmosis was deemed harmless from a health standpoint. However, a range of both indirect and direct evidence, largely amassed over the past decade, has indicated that this perception is misaligned and that latent toxoplasmosis likely exerts a significant adverse impact on physical health. Despite this, subsequent findings suggest that this decline in health is probably not the primary cause of most behavioral changes observed in infected individuals.

Indirect Evidence of Deteriorated Health and Chronic Stress in Infected Individuals

The potential link between latent toxoplasmosis and deteriorated physical health was originally proposed based on the observation that a range of behavioral and personality changes associated with toxoplasmosis have opposite directions in men and women, for review see (Flegr, 2013). For instance, a study employing a series of behavioral experiments demonstrated that infected men scored significantly lower than uninfected men in composite behavioral variables of Clothes-Tidiness (which evaluates subjects' clothing) and Self-Control (which assesses regard for rules, care for personal appearance, orderliness, reliability, and conscientiousness). Conversely, infected women scored higher than uninfected controls on these same variables. A similar trend was observed for the composite behavioral variable of Relationships (which pertains to the quality and quantity of interpersonal relationships) in women, while infected men scored significantly lower than uninfected men on this variable.

The study postulated that these observed sex-specific behavioral differences, as well as numerous sex specific shifts in personality traits previously linked with toxoplasmosis, could be attributed to the deterioration of physical health induced by *Toxoplasma*. More specifically, the study suggested that long-term, mild, and non-specific stress, associated with health deterioration caused by *Toxoplasma*, could be the underlying mechanism driving the contrasting reactions observed in men and women to latent toxoplasmosis. This interpretation draws on a psychological theory of stress coping, which suggests that men and women cope with chronic stress in different ways. According to this theory, men tend to withdraw and seek help less frequently, while women are more likely to seek out social contact and assistance, and also to provide help to others (Lindová et al., 2006).

Another indirect piece of evidence for the deteriorating health status of individuals with latent toxoplasmosis is the gradual decrease in the secondary sex ratio (the ratio of male to female births) among the offspring of infected women. While more sons are born to women (and laboratory-infected mice) immediately following infection, this ratio shifts over time, leading to significantly more daughters being born. The increased secondary sex ratio immediately post-infection, with up to 260 sons being born for every 100 daughters, can be explained by the fact that *Toxoplasma* reduces or shuts down some mechanisms of embryo quality control.

Consequently, this not only leads to the birth of more offspring with developmental defects, but also a greater number of male offspring whose embryos are more immunogenic due to the presence of surface Y-antigens (Kaňková et al., 2007).

As time from infection increases and antibody levels decrease, the sex ratio also diminishes, so that daughters significantly outnumber sons among the offspring of those individuals with the most extended period since infection. This effect is so potent that it is noticeable at the population level. A comparative study conducted in 94 countries demonstrated that the prevalence of toxoplasmosis is the third strongest factor (of the 13 observed) explaining the ratio of sons to daughters born (following son preference and fertility) (Dama et al., 2016). The higher the prevalence of toxoplasmosis in a country, the lower its secondary sex ratio, meaning more daughters are born.

The authors of these studies suggest that the observed decrease in sex ratio, which tends to occur over time since infection, can be attributed to the gradual deterioration in the health of infected women. As stated above, this trend is typically more pronounced in countries with higher toxoplasmosis prevalence. Based on the premises of the Trivers-Willard effect, a it can be proposed that a it can be proposed that a greater number of daughters, on average, are born to women who have been infected for a long term and are therefore in poorer health.

Direct Evidence of Deteriorated Health and Chronic Stress in Infected Individuals

Several cross-sectional studies provided direct evidence that *Toxoplasma*-infected individuals tend to have poorer health. In particular, a large-scale study involving 1486 volunteers found that individuals infected with *Toxoplasma* ($n = 333$) reported worse outcomes across 28 out of 29 health-related variables, compared to those who were uninfected ($n = 1153$) (Flegr & Escudero, 2016). The study noted that the negative effects of toxoplasmosis were most pronounced in the musculoskeletal system, followed by the neurological, immunological, metabolic, respiratory, immune, and digestive systems of the infected subjects.

Further direct evidence of deteriorated health in individuals with latent toxoplasmosis was provided by a correlational study conducted across 88 countries (Flegr et al., 2014). This study also included an extensive review of published clinical studies that depicted the negative impacts of latent toxoplasmosis on the health of infected individuals. The study used data related to mortality and disease-specific burden, estimated through age-standardized Disability-Adjusted Life Years (DALY) for 128 diseases, systematically tracked and published by the World Health Organization (WHO).

The results showed that out of the 128 diseases and disease categories analyzed from the WHO list, 23 showed correlations (18 positive, 5 negative) with the prevalence of toxoplasmosis, while another 12 diseases displayed positive trends ($p < 0.1$). In addition, the prevalence of toxoplasmosis was found to correlate with the specific disease burden in individual countries, accounting for 23% of the variability in disease burden between countries across Europe.

Current Evidence: Refuting the Conventional Health Deterioration Perspective

There is currently only one study directly testing whether or not behavioral changes in infected individuals are merely side effects of deteriorated health (Flegr et al., 2023). This study showed that, although infected subjects had more impaired physical and mental health than uninfected

controls, significant negative associations remained between *Toxoplasma* infection and conscientiousness, injury disgust, and machiavellianism even after controlling for sex, age, and the subjects' mental and physical health. Similarly, the negative associations between *Toxoplasma* infection and both pathogen disgust and tribalism remained significant even after controlling for these factors, although not after correction for multiple tests. Path analysis confirmed the results for all examined behavioral variables significantly associated with *Toxoplasma* infection. It showed that neither physical nor mental health mediated these associations. Based on these findings, the study concluded that the results of multivariate nonparametric tests and path analyses contradicted the hypothesis that the behavioral changes observed in *Toxoplasma*-infected subjects are merely the side effects of impaired health.

Current Insights into *Toxoplasma gondii*'s Impact on Host Hormonal and Neurotransmitter Systems

For several years now, scientists have been interested in the molecular mechanisms through which *Toxoplasma* influences its intermediate hosts. In this section, we will briefly introduce the mechanisms that are relevant to behavioral phenomena. For a more detailed review of the molecular mechanisms of *Toxoplasma*, we refer readers to the reviews by Tong et al. (2021) and Yin et al. (2022).

Testosterone Hypothesis

One of the mechanisms involves hormonal alterations induced by *Toxoplasma* in the intermediate host (Tong et al., 2021); *Toxoplasma* shows a preference for organs with immune privilege, including the brain, eyes, and testes. For instance, *Toxoplasma* cysts have been identified in the ejaculates of several species such as rats. This review also points out that *Toxoplasma* can increase the synthesis of testosterone in the testes of infected males. Testosterone, which reduces fear and anxiety, is a crucial hormonal mediator for *Toxoplasma* to implement its behavioral modifications in infected male hosts. Castration was found to prevent *Toxoplasma*-related behavioral changes. However, it remains uncertain how this parasite manages to alter the behavior of infected females that do not have testes (Tong et al., 2021).

Dopamine and Dopamine-Norepinephrine Hypothesis

The potential association between elevated dopamine levels and both the behavioral manifestations of latent toxoplasmosis and increased schizophrenia risk in *Toxoplasma*-infected subjects was suggested in a study by Flegr et al. (2003). The authors profiled the personalities of 857 military conscripts, both infected and uninfected with *Toxoplasma*, using Cloninger's Temperament and Character Inventory. The study revealed that infected individuals had lower levels of the Novelty Seeking factor, which, according to psychopharmacological studies, negatively correlates with dopamine levels. Based on these findings, and considering that dopamine elevation heightens the risk of schizophrenia – and particularly its positive symptoms – the authors hypothesized that certain behavioral manifestations of latent toxoplasmosis, as well as the connection between toxoplasmosis and schizophrenia, could be attributable to increased dopamine levels.

Tong et al. (2021), based on the findings of related studies, detail how *Toxoplasma*-induced neurotransmitter alterations in the intermediate host contribute to the behavioral pathology of toxoplasmosis. According to this review, *Toxoplasma* genome contains two genes that encode for amino acid hydroxylase, a key rate-limiting enzyme in dopamine synthesis. This suggests that *Toxoplasma* can elevate dopamine levels in the brain. Researchers have also found that dopamine plays a role in pleasure and motivation. Additionally, *Toxoplasma* appears to increase the synthesis of arginine vasopressin in the medial amygdala, a region involved in motivation and perception of sexual pheromones (see Hari Dass & Vyas, 2014). According to the review, either an upregulation of dopamine, an increase in arginine vasopressin synthesis, or both, could explain observed

behavioral changes such as reduced fear, recklessness, and impulsivity in infected intermediate hosts (particularly rodents). These behavioral changes echo those reported in infected humans discussed earlier in the present article. For instance, the effects of toxoplasmosis on entrepreneurship activity, including a diminished fear of failure, and personality shifts such as increased extraversion, lower conscientiousness, and a disregard for rules in *Toxoplasma*-infected men, support the dopamine hypothesis.

In reference to the role of dopamine, another review discusses the pathophysiology of toxoplasmosis in the intermediate host through the lens of the dopamine-norepinephrine hypothesis. According to this hypothesis, *Toxoplasma* modulates the expression of a gene for dopamine B-hydroxylase (DBH), the enzyme responsible for the synthesis of norepinephrine. The review reports that this results in a decrease in norepinephrine levels in both human and rat neurons cultured in vitro. As also pointed out by the review, it has been demonstrated that the down-regulation of DBH is indeed associated with behavioral change (Yin et al., 2022).

Neuroinflammation Hypothesis

In a study examining the relationship between *Toxoplasma* and personality change, local neuroinflammation was proposed as a crucial component in the pathophysiology of *Toxoplasma*-induced personality shifts (see Novotná et al., 2005).

Tong et al. (2021) provide a review of this mechanism. According to this review, based on the related study findings, immune system activity is essential for limiting acute toxoplasmosis. In addition, inflammation is reported to mediate *Toxoplasma*-induced behavioral effects. Interestingly, guanabenz, an anti-inflammatory drug, can mitigate *Toxoplasma*-induced behavioral effects. The review argues that most studies examining these behavioral changes in the context of the neuroinflammation theory suggest these modifications are not specific to cat odor, but instead represent non-specific, multifaceted effects brought about by continuous immune challenge.

Yin et al. (2022) also discuss *Toxoplasma*-induced neuroinflammation and its relationship with impaired neuronal functioning. Based on the findings reported in the related studies, they argue that in response to *Toxoplasma* infection, the host's immune response triggers chemokines such as interferon-inducible protein 10 (IP-10) and monocytic chemotactic protein 1 (MCP-1), as well as cytokines like interleukin (IL)-1b, IL-6, and tumor necrosis factor alpha (TNF-α). These chemokines and cytokines either directly impact neurons or recruit macrophages and monocytes into the brain, impairing neuronal functioning. This may subsequently alter neurotransmitter levels in the brain, resulting in the specific manipulation effects observed in the infected intermediate host.

Serotonin/GABA Hypothesis

The serotonin/GABA Hypothesis suggests that *Toxoplasma* can interfere with the regulation of KYNA, 5-HT, and GABA, which play critical roles in disorders related to fear, anxiety, and cognition. Yin et al. (2022) delve into this in their review of toxoplasmosis pathophysiology. They postulate, based on findings from pertinent studies, that a *Toxoplasma* infection elicits the host's immune response, activating CD^{8+}/CD^{4+} T cells that stimulate astrocytes and microglia. These, in turn, produce inflammatory cytokines like IL-6, IL-1b, and TNF-α within the brain tissue.

The activated astrocytes can degrade tryptophan, transforming it into kynurenic acid (KYNA). KYNA can inhibit the activity of the acetylcholine receptor (AchR) and the glutamate receptor (NMDAR), which can negatively affect the cognitive functioning of the host. The review continues to illustrate how *Toxoplasma*, via the KYNA pathway, can disrupt the synthesis of 5-hydroxytryptamine (5-HT).

Furthermore, *Toxoplasma* is capable of metabolizing gamma-aminobutyric acid (GABA), a crucial inhibitory neurotransmitter in the brain that regulates fear, anxiety, and the balance between excitatory and inhibitory neural activities. The parasite has the ability to influence the GABAergic signaling pathway, inducing

hypermigration of dendritic cells and microglia, which in turn facilitates parasite dispersion in the brain and the loss of inhibitory synapses. The parasite may also enhance the distribution of glutamate decarboxylase 67 (GAD67), a synthetase of GABA, thereby influencing the host's behavior.

Epigenetic Regulation

Yin et al. (2022) discuss another crucial mechanism involved in *Toxoplasma*-induced behavioral modifications: epigenetic regulation. According to this review, epigenetics serves as a bridge between intrinsic genetic factors and extrinsic environmental determinants, making it well-suited to study the complex interactions between the parasite and its host. The review highlights studies showing that *Toxoplasma* can introduce specific effectors into the host's cells to regulate gene expression and potentially influence the host's immune system.

Moreover, the reviewers explore the epigenetic regulatory mechanism responsible for the previously discussed "fatal attraction" phenomenon. As noted earlier, *Toxoplasma* infection triggers hypomethylation of the promotor for the host's arginine vasopressin gene in the medial amygdala of infected mice. The subsequent increase in gene expression leads to heightened testosterone secretion, which the review suggests can trigger attraction to cat urine odor. However, the review also points out that these testosterone-related mechanisms don't fully explain the behavioral changes observed in infected female hosts, thus suggesting a need for future research to focus on female hormones such as oxytocin.

The review further discusses other *Toxoplasma*-induced epigenetic processes, such as the downregulation of DBH expression leading to decreased norepinephrine levels in infected hosts, as well as *Toxoplasma*'s interference with two vital pathways (the dopamine-DARPP32 feedback pathway and the amyloid protein pathway), both associated with conditions like schizophrenia, Alzheimer's disease, and Parkinson's disease.

Conclusion

This entry primarily offers a summary of meta-analyses and reviews on the subject of behavioral impacts of the *Toxoplasma* infection in both animal models and human studies. Throughout their long co-evolutionary journey, parasites and their hosts have developed intricate mechanisms to manipulate each other, with *Toxoplasma* displaying some of the most nuanced techniques to enhance its transmission probability. Following infection, the parasite manipulates the intermediate host's behavior to increase the likelihood of being ingested by the definitive host, a crucial stage for the completion of the parasite's life cycle. These manipulations result in alterations like reduced neophobia, diminished fear or even attraction to predators, increased mobility, slower information processing, impaired learning and memory, and hindered executive functions. Moreover, *Toxoplasma* infection can trigger shifts in the human personality profile, with some changes appearing to be sex-specific. The infection also poses a risk factor for various psychiatric disorders, including schizophrenia, OCD, and bipolar disorder.

Interestingly, the parasite's evolutionary strategies seem to significantly impact sexual behavior, a vital arena that helps to increase its transmission probability. This is especially important considering the potential sexual transmission of *Toxoplasma* infection, along with behaviors accompanying or concurrent with sexual activity in some species, including humans.

While the physiological mechanisms behind these *Toxoplasma*-induced behavioral and cognitive changes remain largely unknown, it's likely that a combination of mechanisms is at play. These may involve alterations in hormonal levels (particularly testosterone in males and possibly estrogen or oxytocin in females), changes in neurotransmitter levels (mainly dopamine, followed by serotonin, norepinephrine, and GABA), immune responses to the infection, and direct physical and anatomical damage to the central nervous system.

From an evolutionary perspective, these manipulations seem to align with the parasite's transmission goals. They typically fall into two categories: those that make it more likely for the intermediate host to be preyed on by the definitive host, and those that facilitate the sexual transmission of the parasite, either horizontally (male to female during intercourse) or vertically (from the infected mother to the offspring).

In conclusion, it is crucial to underscore that pathogen-induced alterations in host behavior could be far more common than currently recognized (refer also to the chapter Xenoadaptation). *Toxoplasma* may be just one of many pathogens subtly shaping our behavior, cognition, emotions, and more, both individually and societally. Its identification as a significant pathogen affecting human behavior is largely due to the dedicated research teams studying it over the past three decades. If similar research efforts were directed toward other pathogens, we might discover their influence on human behavior to be even more profound. The case of *Toxoplasma* mainly illustrates that the impact of seemingly asymptomatic latent infections on human behavior, mental health, and well-being could be far more substantial than we have so far been willing to acknowledge.

Cross-References

- ▶ Manipulation Hypothesis
- ▶ Trivers-Willard Effect
- ▶ Good Genes Hypothesis
- ▶ Good Parents Hypothesis
- ▶ Stress Coping
- ▶ Evolutionary Parasitology
- ▶ Postadaptation
- ▶ Xenoadaptation

References

Barnard, C. J., & Behnke, J. M. (Eds.). (2005). *Parasitism and host behaviour*. Taylor & Francis e-Library. (Originally published in 1990).

Berdoy, M., Webster, J. P., & Macdonald, D. W. (2000). Fatal attraction in rats infected with *Toxoplasma gondii*. *Proceedings of the Royal Society of London Series B: Biological Sciences, 267*(1452), 1591–1594. https://doi.org/10.1098/rspb.2000.1182

Borráz-León, J. I., Rantala, M. J., Krams, I. A., Cerda-Molina, A. L., & Contreras-Garduño, J. (2022). Are *Toxoplasma*-infected subjects more attractive, symmetrical, or healthier than non-infected ones? Evidence from subjective and objective measurements. *PeerJ, 10*, e13122. https://doi.org/10.7717/peerj.13122

Dama, M. S., Novakova, L. M., & Flegr, J. (2016). Do differences in *Toxoplasma* prevalence influence global variation in secondary sex ratio? Preliminary ecological regression study. *Parasitology, 143*(9), 1193–1203. https://doi.org/10.1017/S0031182016000597

de Haan, L., Sutterland, A. L., Schotborgh, J. V., Schirmbeck, F., & de Haan, L. (2021). Association of *Toxoplasma gondii* seropositivity with cognitive function in healthy people: A systematic review and meta-analysis. *JAMA Psychiatry, 78*(10), 1103–1112. https://doi.org/10.1001/jamapsychiatry.2021.1590

Flegr, J. (2013). Influence of latent *Toxoplasma* infection on human personality, physiology and morphology: Pros and cons of the *Toxoplasma*–human model in studying the manipulation hypothesis. *Journal of Experimental Biology, 216*(1), 127–133. https://doi.org/10.1242/jeb.073635

Flegr, J., & Escudero, D. Q. (2016). Impaired health status and increased incidence of diseases in *Toxoplasma*-seropositive subjects–an explorative cross-sectional study. *Parasitology, 143*(14), 1974–1989. https://doi.org/10.1017/S0031182016001785

Flegr, J., & Kuba, R. (2016). The relation of *Toxoplasma* infection and sexual attraction to fear, danger, pain, and submissiveness. *Evolutionary Psychology, 14*(3). https://doi.org/10.1177/1474704916659746

Flegr, J., Preiss, M., Klose, J., Havlíček, J., Vitáková, M., & Kodym, P. (2003). Decreased level of psychobiological factor novelty seeking and lower intelligence in men latently infected with the protozoan parasite *Toxoplasma gondii* dopamine, a missing link between schizophrenia and toxoplasmosis? *Biological Psychology, 63*(3), 253–268. https://doi.org/10.1016/S0301-0511(03)00075-9

Flegr, J., Hrušková, M., Hodný, Z., Novotná, M., & Hanušová, J. (2005). Body height, body mass index, waist-hip ratio, fluctuating asymmetry and second to fourth digit ratio in subjects with latent toxoplasmosis. *Parasitology, 130*(6), 621–628. https://doi.org/10.1017/S0031182005007316

Flegr, J., Preiss, M., & Klose, J. (2013). Toxoplasmosis-associated difference in intelligence and personality in men depends on their rhesus blood group but not ABO blood group. *PLoS One, 8*(4), e61272. https://doi.org/10.1371/journal.pone.0061272

Flegr, J., Prandota, J., Sovickova, M., & Israili, Z. H. (2014). Toxoplasmosis – A global threat. Correlation of latent toxoplasmosis with specific disease burden in

a set of 88 countries. *PLoS One, 9*(3), e90203. https://doi.org/10.1371/journal.pone.0090203

Flegr, J., Hlavacova, J., & Toman, J. (2023). Parasitic manipulation or side effects? The effects of past *Toxoplasma* and *Borrelia* infections on human personality and cognitive performance are not mediated by impaired health. *Folia Parasitologica, 70*, 020.

Hari Dass, S. A., & Vyas, A. (2014). *Toxoplasma gondii* infection reduces predator aversion in rats through epigenetic modulation in the host medial amygdala. *Molecular Ecology, 23*(24), 6114–6122. https://doi.org/10.1111/mec.12888

Hari Dass, S. A., Vasudevan, A., Dutta, D., Soh, L. J. T., Sapolsky, R. M., & Vyas, A. (2011). Protozoan parasite *Toxoplasma gondii* manipulates mate choice in rats by enhancing attractiveness of males. *PLoS One, 6*(11), e27229. https://doi.org/10.1371/journal.pone.0027229

Hlaváčová, J., Flegr, J., Řežábek, K., Calda, P., & Kaňková, Š. (2021). Male-to-female presumed transmission of toxoplasmosis between sexual partners. *American Journal of Epidemiology, 190*(3), 386–392. https://doi.org/10.1093/aje/kwaa198

Hodková, H., Kolbeková, P., Skallová, A., Lindová, J., & Flegr, J. (2007). Higher perceived dominance in *Toxoplasma* infected men–a new evidence for role of increased level of testosterone in toxoplasmosis-associated changes in human behaviour. *Neuroendocrinology Letters, 28*(2), 110–114.

House, P. K., Vyas, A., & Sapolsky, R. (2011). Predator cat odors activate sexual arousal pathways in brains of *Toxoplasma gondii* infected rats. *PLoS One, 6*(8), e23277. https://doi.org/10.1371/journal.pone.0023277

Johnson, S. K., & Johnson, P. T. (2021). Toxoplasmosis: Recent advances in understanding the link between infection and host behaviour. *Annual Review of Animal Biosciences, 9*, 249–264. https://doi.org/10.1146/annurev-animal-081720-111125

Johnson, S. K., Fitza, M. A., Lerner, D. A., Calhoun, D. M., Beldon, M. A., Chan, E. T., & Johnson, P. T. (2018). Risky business: Linking *Toxoplasma gondii* infection and entrepreneurship behaviours across individuals and countries. *Proceedings of the Royal Society B: Biological Sciences, 285*(1883), 20180822. https://doi.org/10.1098/rspb.2018.0822

Kaňková, Š., Šulc, J., Nouzová, K., Fajfrlík, K., Frynta, D., & Flegr, J. (2007). Women infected with parasite *Toxoplasma* have more sons. *Naturwissenschaften, 94*, 122–127. https://doi.org/10.1007/s00114-006-0166-2

Lindová, J., Novotná, M., Havlíček, J., Jozífková, E., Skallová, A., Kolbeková, P., et al. (2006). Gender differences in behavioural changes induced by latent toxoplasmosis. *International Journal for Parasitology, 36*(14), 1485–1492. https://doi.org/10.1016/j.ijpara.2006.07.008

Lindová, J., Kubena, A. A., Šturcová, A., Krivohlavá, R., Novotná, M., Rubešová, A., et al. (2010). Pattern of money allocation in experimental games supports the stress hypothesis of gender differences in *Toxoplasma gondii*-induced behavioural changes. *Folia Parasitologica, 57*, 136–142.

Maisarah, A., Mohamad, S., Husain, M., Abdullah, S., & Noordin, R. (2022). Association between infection with *Toxoplasma gondii* and psychiatric disorders. *Folia Parasitologica, 69*, 1–10. https://doi.org/10.14411/fp.2022.008

Martinez, V. O., de Mendonça Lima, F. W., De Carvalho, C. F., & Menezes-Filho, J. A. (2018). *Toxoplasma gondii* infection and behavioural outcomes in humans: A systematic review. *Parasitology Research, 117*, 3059–3065. https://doi.org/10.1007/s00436-018-6040-2

Novotná, M., Hanusova, J., Klose, J., Preiss, M., Havlicek, J., Roubalová, K., & Flegr, J. (2005). Probable neuroimmunological link between *Toxoplasma* and cytomegalovirus infections and personality changes in the human host. *BMC Infectious Diseases, 5*(1), 1–10. https://doi.org/10.1186/1471-2334-5-54

Sutterland, A. L., Fond, G., Kuin, A., Koeter, M. W. J., Lutter, R., Van Gool, T., et al. (2015). Beyond the association. *Toxoplasma gondii* in schizophrenia, bipolar disorder, and addiction: Systematic review and meta-analysis. *Acta Psychiatrica Scandinavica, 132*(3), 161–179. https://doi.org/10.1111/acps.12423

Tong, W. H., Pavey, C., O'Handley, R., & Vyas, A. (2021). Behavioural biology of *Toxoplasma gondii* infection. *Parasites & Vectors, 14*, 77. https://doi.org/10.1186/s13071-020-04528-x

Torrey, E. F., Bartko, J. J., & Yolken, R. H. (2012). *Toxoplasma gondii* and other risk factors for schizophrenia: An update. *Schizophrenia Bulletin, 38*(3), 642–647. https://doi.org/10.1093/schbul/sbs043

Yin, K., Xu, C., Zhao, G., & Xie, H. (2022). Epigenetic manipulation of psychiatric behavioural disorders induced by *Toxoplasma gondii*. *Frontiers in Cellular and Infection Microbiology, 12*, 59. https://doi.org/10.3389/fcimb.2022.803502