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Toxoplasma Gondii Protozoan Parasite induced behavioral changes in Humans and Wild Animals: A Comprehensive Analysis

Dr. Arun Kumar^{*1}, Vinay Kumar¹, Dr. Sebu², Sanchit Yadav³

Assistant Professor, BBDIT College of Pharmacy, Ghaziabad (India)¹

Assistant Professor, Mesco Institute of Pharmacy, Amroha (India)²

Student, Bachelor of Pharmacy, BBDIT College of Pharmacy, Ghaziabad (India)³

ABSTRACT: A complicated life cycle and a global host range characterize *Toxoplasma gondii*, a protozoan parasite. Only after predating on infected intermediate hosts does *T. gondii* create gametes in felids. The parasite modifies the behavior of its intermediate hosts by decreasing their natural aversion to cat odors, which may increase the likelihood that the final host would eat the infected host. *T. Gondii* has three infectious stages: tachyzoites, bradyzoites, and sporozoites. Oocysts or bradyzoites are the primary means of infection for both humans and animals. In the tissues after ingestion, sporozoites and bradyzoites transform into tachyzoites. Because bradyzoites are less sensitive to chemotherapy and because the reactivation of bradyzoites to tachyzoites is thought to be the cause of deadly toxoplasmosis, the conversion is significant from a biological and clinical standpoint. The most dependable approach involves feeding cats *T. Gondii* infective stages for stage conversion. The *T. gondii* hosts, Felidae, expel oocysts 3–10 days after consuming tissue cysts, bradyzoites more than 18 days after consuming oocysts, and tachyzoites more than 13 days after swallowing. Beyond the physical boundaries of each parasite body, the parasite genes can produce a phenotypic. The mechanism of *T.gondii* stage change may be studied with the use of specific antibodies and molecular marker methods. Once established, it can interfere with amino acid hydroxylase and enhance the availability of dopamine-containing medications in the brain. Additionally, it is in charge of the medial amygdala's elevated arginine and vasopressin production. The quantity of cysts in the host's brain determines how much the animal behaves differently.

KEYWORDS: Toxoplasmosis, BAG-4 Antibody, ME-49 Strain, Dopamine, Vasopressin, Medial Amygdala, Parasitophorous Vacuole.

I. INTRODUCTION

WHAT IS TOXOPLASMA GONDII?

Enteric coccidian *Toxoplasma gondii* is an intracellular parasite that conducts sexual reproduction to create oocysts in the small intestine of cats, its ultimate host. This is where the parasite completes its life cycle. The feces of the sick cat expel these oocysts, which have a diameter of 11–13 μm . The sporulated oocysts that are consumed by an intermediate host after their development in the environment, known as sporulation, release sporozoites, which are the intestinal and lymph node cells where they change into a rapidly dividing asexual stage known as a tachyzoite. The tachyzoites spread to various bodily regions. [1-2]. Acute toxoplasmosis is caused by their fast proliferation and subsequent host cell death, which is shown as moderate to severe clinical symptoms. After this acute phase, tissue cysts comprising a stage of sluggish reproduction of bradyzoites develop. These tissue cysts can remain in the brain, liver, or muscles throughout the duration of the intermediate host's life. A tachyzoite infection during pregnancy has the potential to spread vertically to the developing baby. Exposure occurs often in humans, with an estimated exposure rate of between 30 and 35%. Rates can vary from 10 to 80% in some cultures and are impacted by dietary choices and behavior. [3-4].

GENERAL BIOLOGY OF T. GONDII

Toxoplasma gondii infections are common in both humans and animals. The two main routes of postnatal transmission of *T. gondii* are ingestion of food or water contaminated with oocysts from cat feces or ingestion of tissue cysts in undercooked meat. Tachyzoites proliferate in a range of cells upon infection with any infectious stage and ultimately encyst in several organs, most notably the brain. In the brain, tissue cysts last a very long period. According to a theory,

tissue cysts periodically burst, and the bradyzoites that are discharged kill immunocompetent hosts [5-6]. However, bradyzoites generated from tissue cysts may grow locally and spread to other organs of the body in immune-compromised hosts, such as AIDS patients. The most common clinical sign of toxoplasmosis in individuals with AIDS is encephalitis. Chemotherapy that works well against tachyzoites is less effective against bradyzoites. Thus, the destiny of bradyzoites inside their host tissues holds clinical importance. There are several factors that separate tachyzoites from bradyzoites. Tachyzoites are structurally composed of a core nucleus. Bradyzoites contain a terminal nucleus; during the chronic phase, they are more common. Periodic acid schiff (PAS)-positive granules are surrounded by a resistant cyst wall [7-8]

EFFECTS ON HOST BEHAVIOUR

A rat raised in a lab will avoid the corner of a box containing a few drips of cat pee if it is placed there. In addition, the rat will release stress hormones, become more alert, and experience less discomfort. Rats are naturally afraid of signs that indicate cats are around. Even the odor attracts some diseased rats. Put another way, *T. gondii* turns a natural dread of rats into a desire [9-10]. The most widely accepted hypothesis holds that a courageous rat is more likely to be eaten by a cat, which is advantageous for *T. gondii* since it develops gametes in the cat, the final host, and excretes environmentally stable oocysts in the form of feces. To enhance its transmission, *T. gondii* thus modifies the host's behavior. The model of parasite behavior manipulation known as the Rodent-*T. gondii* paradigm is one of the most researched. There are three basic categories into which *T. gondii* infection-related behavioral consequences may be divided. Firstly, some research indicates that the effects of *T. gondii* are mostly focused on preventing cats from smelling like cats or predators, which is not crucial for the parasite's life cycle to be less affected by the manipulative effects of the [11-12]. According to a second set of research, the consequences are syndromic, meaning that the infection results in the host's loss of a variety of protective behaviors. Therefore, even if human-built traps differ from those constructed by cats, trap skill still grows. Rats with the infection become more impulsive, risk-takers, and adventurous. According to a third set of research, *T. gondii* induces a behavioral fever-like illness that involves a variety of behavioral abnormalities that are inappropriate for the host, and the confluence of these abnormalities may make cats more likely to prey on humans [13]. The particular *T. gondii* strains and rodent species employed in the investigation account for a significant portion of this variety. The four clonal lineages Type-I, II, III, and XII contain the bulk of the genetic variation seen in *T. gondii*. Rats infected with less virulent type-II strains usually exhibit more targeted behavioral effects during the chronic phase of the illness, with lesser magnitude sickness behaviors during the acute phase. Though type-II strains account for the bulk of infections in humans and cattle globally. Outbred rats infected with *T. gondii* showed highly precise behavioral effects with few signs of illness [14-15].

LIFE CYCLE IN CATS

The definitive host (Felidae) and intermediate host (humans, mice) have different life cycles for *T. gondii*. For three to ten days following the consumption of bradyzoites, felidae excrete *T. gondii* oocysts in their feces. The cat bradyzoite-induced cycle is the most effective as almost all of the cats consumed tissue cysts. On the other hand, almost 30% of the cats given tissue cysts shed oocysts [16]. Compared to intermediate hosts (mice, pigs, and humans), *T. gondii* oocysts are less harmful and less infectious in their final host, cats. The cat's gut produces millions of oocysts due to the widespread proliferation of *T. gondii* [17-18]. Five morphologically different asexual kinds are generated in feline enterocytes following the consumption of bradyzoites, which triggers a sexual cycle that produces oocytes. According to one theory, *T. gondii* invades a variety of cat tissues following oocyst intake, and bradyzoites created in extra intestinal tissue return to the intestine to start the bradyzoite-induced coccidian cycle. After ingesting oocysts, only few cats undergo the entire coccidian cycle [19]. The parasite mostly modifies the host's behavior and boosts the effectiveness of transmission. A phenotype that is not limited by the physical boundaries of the parasite's particular body can be caused by its genes [20-21].

OOCYST-INDUCED CYCLE IN THE INTERMEDIATE HOST AFTER ORAL INGESTION

Mice that consume oocysts may perish if they develop multiple enteritis before another organ becomes badly parasitized. Within 30 minutes of the oocysts eating, sporozoites are seen in a portion of the tiny intestine enterocytes. Most sporozoites can form a parasitophorous vacuole (PV) in enterocytes within two hours after swallowing oocysts. The lamina propria, infected capillary endothelial cells, macrophages, plasma cells, lymphocytes, neutrophils, eosinophils, smooth muscle cells, and fibroblasts are the primary locations where sporozoites are seen at 6 hrp.i. [22-23]. 48-72 hours postpartum, tachyzoites arising from the lamina propria infect the enterocytes. Parasitemia can also be found in certain mice as early as 3 hrp.i, however 48 hrp.i is when it is most frequently found. I. Several extraintestinal organs are expected to get infected three days following the vaccination. According to the results of bioassays conducted on cat murine organs, bradyzoites develop five to six days after oocyst infection. Depending on the strain

and dosage of *T. gondii* given to the mice, the oocysts perished in the first week of pneumonia from enteritis, and in the second and third weeks from encephalitis and pneumonia. The primary lesion in mice who died four weeks after consuming oocysts was encephalitis [24-25].

BRADYZOITE-INDUCED CYCLE IN INTERMEDIATE HOSTS

It is possible to compare the destiny of bradyzoites with infections caused by oocysts by seeing how they feed on tissue cysts or bradyzoites. For mice that have been infected orally, *T. gondii* bradyzoites are less harmful and less infectious. The only way to infect mice consistently is to feed them 1000 infective bradyzoites [26]. These findings suggest that the gut lumen has a role in the destruction of certain bradyzoites. Within eighteen hours of ingestion, bradyzoites can transform into tachyzoites in the small intestine lamina propria. Following that, tachyzoites moved to extraintestinal organs [27-28].

RESISTANCE OF *T. GONDII* TACHYZOITES AND BRADYZOITES TO PEPSIN AND TRYPSIN DIGESTION

Bradyzoites are more contagious because they are resistant to stomach digestion. Gastric juice annihilates tachyzoites that are taken orally. The enzymes used to differentiate tachyzoites from bradyzoites affect *T. gondii* tachyzoites both in vitro and in vivo in response to trypsin and pepsin. Tachyzoites are frequently destroyed within 30 minutes in an acid pepsin solution [29]. In vitro, some extracellular tachyzoites of *T. gondii* may last for two hours in acid pepsin. Mice are given oral tachyzoites of the RH strain of *T. gondii* for in vivo experiments, and it is discovered that dosages of 1000 extracellular tachyzoites of *T. gondii* are contagious. The cats who are given tachyzoites of a strain of *T. gondii* that produces oocysts (VEG) get infected and shed oocysts. A youngster that was given unpasteurized goat milk has been documented to have toxoplasmosis [30-32].

FORMATION AND PERSISTENCE OF TISSUE CYSTS IN ANIMALS

Bradyzoites, or tissue cysts, are an essential component of *T. gondii*'s life cycle. Although they are formed early in the infection process, tissue cysts predominate after chronic infection. Usually, tissue cysts develop five to six days after eating bradyzoites and seven to eight days after consuming oocysts. Gastric juice has a greater ability to break down the early tissue cysts known as bradyzoites. Animal hosts and *T. Gondii* strains vary in the location and quantity of tissue cysts. The brain has more tissue cysts in mice and rats than the visceral tissues [33-35].

COMPARISON OF IN VIVO AND IN VITRO STUDIES

The process of *T. Gondii*'s stage change may now be studied thanks to the development of molecular marker methods and stage-specific antibodies. Tissue cysts are generated by 3 days post-immunization (p.i.) of human foreskin fibroblasts with bradyzoites of the ME-49 strain, according to research using the BAG-4 antibody. Certain bradyzoites seem to create tissue cysts directly without changing into tachyzoites [36]. Tissue cysts were found in human foetal neuronal culture with the ME-49 strain starting at 2 days hrp.i., which was contrary to the findings of in vitro experiments. By 18 hrp.i., all bradyzoites had transformed into physiologically defined tachyzoites, and by 48 hrp, the organisms had turned BAG-5 negative. In cell culture, *T. gondii* sporozoites generate two forms of PV. The first vacuole (PV1) lacked a membrane network and was 10–15 times larger than the sporozoite [37-38].

WHY DO WE NEED TO STUDY THE NATURAL SCIENCE OF PARASITE?

The link between parasitism and host behavior has long piqued the curiosity of biologists, since parasites have been used to explain why heritable sexual advertisements persist in males. The idea of extended phenotypes frequently makes advantage of parasites' ability to manipulate host behaviour [39]. Many parasites change the way they behave in their hosts, maybe to increase the effectiveness of their spread. Thus, even when a parasite is not physically present in its body, its genes can nonetheless influence its phenotype. Testable hypotheses about extended phenotypes may be tested in an experimentally feasible setting using laboratory mice infected with *T. Gondii* [40]. Additionally, behavioral neurobiologists might utilize the *T. gondii* paradigm in the same manner that geneticists can to comprehend intrinsic anxiety. Because the biology of fear and mental disorders like post-traumatic stress disorder are related, this research is crucial. Bipolar disorder, obsessive-compulsive disorder, and schizophrenia are among the mental illnesses that *T. gondii* raises the risk of acquiring. Because they create variability in the chance of consuming infected vs non-infected prey, manipulative parasites like *T. gondii* are likely to alter such cascades [41-42].

A) THREE ADVANCES IN *T. GONDII* BEHAVIOURAL BIOLOGY

There is a clear preference for the brain and eyes in *T. gondii*. Due to their restricted access to immune cells, certain organs are considered immune privileged. The male testes divide growing sperm behind a strong wall that mostly

prevents immune cells from entering. Rat testes are invaded by *T. gondii* after it passes beyond this barrier. Rat ejaculates contain *T. gondii*, which increases the production of testosterone. Because of the way that *T. gondii* interacts with the brain, more testosterone is essential for its effects [43].

B) T. GONDII INFECTION ALTERS NEUROTRANSMISSION WITHIN THE HOST BRAIN

Specific alterations in the chemical messengers used by the brain's inter-neuronal connections are brought about by a persistent infection with *T. gondii*. Two loci with strong similarity to human genes that code for amino acid hydroxylase, a rate-limiting enzyme in dopamine production, are found in the genome of *T. gondii*. Once *T. gondii* is present in the brain, it can make dopamine more readily available [44-45]. The behavioral consequences of *T. gondii* are also mitigated by medications that disrupt the metabolism of dopamine. In addition, arginine and vasopressin are more synthesized in the medial amygdala, a particular area of the brain affected by *T. gondii* infection. These neurons are linked to areas of the brain related to motivation and are involved in the perception of sexual pheromone [46].

C) T. GONDII EFFECTS COULD BE MEDIATED THROUGH NEUROINFLAMMATION

The host immune system is crucial for controlling the acute phase of a *T. gondii* infection, and it also plays a crucial role in modulating the behavioral consequences by preserving encasement inflammation. The amount of behavioral alterations that occur throughout repeated cycles of recrudescence is correlated with the quantity of cysts in the mouse brain and the immunological response that follows. Even *T. gondii* strains that do not result in long-term encasement in the mouse brain can nevertheless control the behavior of their host. By preventing molecular alterations in certain brain areas, behavioral impacts can be salvaged; cyst density is unlikely to be impacted by this therapy [47].

D) THREE OPPORTUNE RESEARCH AREAS

The ability of parasites to alter host behavior provides them with an adaptive advantage in the present. Relevantly, it is uncertain if *T. gondii* raises the likelihood that cats would prey on infected rodents. While gametogenesis necessitates cats, *T. gondii* may survive its asexual period of life without them. Cats eat rodents infected with *T. gondii* more frequently than they do non-infected ones [48].

E) CONSEQUENCES OF THE INFECTION FOR LIFE-HISTORY PLASTICITY

Animals have myopic life histories that favor early reproduction even when doing so comes at the expense of survival in response to an increasing chance of mortality. For instance, Tasmanian devils respond to facial tumour illness by reproducing sooner since the likelihood of surviving during the second or third reproductive cycle is reduced. The host is likely to react with shortened life histories if *T. gondii* raises predation rates [49-50].

F) MAKING SENSE OF DIVERSE HOST-PARASITE COMBINATIONS

There is a great deal of variation in the behavioral effects of *T. gondii* between experiments, particularly when rats and mice are used. In order to construct evolutionary comparisons of behavioural responses to the infection, this gap presents an important study opportunity. It is necessary to show how past parasite selection processes have exerted various influences on host sexual selection. Another interesting field of study that might benefit from the use of genetic crosses of the parasite to map pertinent loci in the parasite genome is the varying impact of *T. gondii* strains on host behaviour [51-52].

G) TOXOPLASMA GONDII: TRANSMISSION, DIAGNOSIS AND PREVENTION

Human infection with *Toxoplasma gondii* is common. Estimates of the prevalence in the United States and the United Kingdom vary from 16–40% of the population, whereas estimates of infection in continental Europe, Central and South America, and Africa reach 50–80%. Congenital infection only happens when an infection develops in a pregnant woman. First trimester congenital infections are more serious than second and third trimester congenital illnesses. Rarely does the mother exhibit signs of transient parasitemia. When the placenta develops focal lesions, the fetus may contract an infection that spreads to the central nervous system after the infection has been eradicated from the visceral tissues. Children with severe condition may have convulsions, hydrocephalus, retinochoroiditis, and intracerebral calcification. Mild disease may only cause mild visual impairment. Ocular illness is the most typical side effect of congenital toxoplasmosis. The socioeconomic effects of toxoplasmosis on those who are ill, particularly in those who are blind or mentally retarded [53]. In France and Austria, testing for *T. gondii* infection is a standard procedure for all expectant mothers. An infection acquired after birth may be localized. Humans can get the infection by consuming food or water tainted with oocysts from infected cat feces, or by consuming tissue cysts found in raw or undercooked meat. illnesses caused by oocysts could be more serious than illnesses brought on by tissue cysts. In humans, the most common clinical manifestation of toxoplasmosis is enlarged lymph nodes. Fever, exhaustion, headache, sore throat, and

muscular soreness are all possible side effects of lymphadenopathy. Out of 100 individuals diagnosed with acute infection during an epidemic in British Columbia, 51 had lymphadenopathy and 20 had retinitis [54].

H) SYMPTOMS

Headache, confusion, fatigue, hemiparesis, altered reflexes, convulsions, and comatose states are among the symptoms that patients may experience. Ten percent of AIDS patients in the United States and thirty percent in Europe die from toxoplasmosis. Testicles, dermis, and spinal cord are among the organs affected in AIDS patients. The headache may eventually give place to ataxia, disorientation, lethargy, and coma as the illness worsens. Necrosis is the most common type of brain damage, particularly in the thalamus [55-56].

I) SOURCES OF CONTAMINATION

Cats living indoors are the main cause of pollution. After consuming just one bradyzoite or one tissue cyst, cats may defecate millions of oocysts, and one infected mouse may have many tissue cysts. After being reinoculated with tissue cysts, around 1% of the cats are seen to be shedding oocysts at any given moment in the experimental setting. In damp soil, sporulated oocysts can last for months or even years [57-58]. Oocysts in the soil can be mechanically dispersed and even carried onto food by insects including dung beetles, flies, cockroaches, and earthworms. Cats are susceptible to congenital infections, and affected kittens may expel oocysts.

- **ANIMALS**

Cat excrement can be examined to find oocysts. The reason flotations in high-density solution are commonly utilized in concentration procedures is that there may not be enough *T. gondii* oocysts in cat feces for a direct smear to identify them. Aquatic animal infections are indicative of oocyst contamination and survival in saltwater. A slaughter operation in Iowa produced 17% of 1000 adult pigs (sows) that tested positive for *T. gondii*. The most common hosts of *T. gondii* infection are white-tailed deer and black bears. Because raccoons and bears scavenge for food, around 60% of raccoons in the United States have antibodies to *T. Gondii*, while about 80% of black bears are infected. These animals' infections are a reliable predictor of *T. gondii* prevalence [59-60]. One tissue cyst is thought to be possible for every 100 grams of meat. Consequently, it is impractical to identify this low level of *T. gondii* infection through the digestion of meat samples without the use of a concentration approach. *T. gondii* in meat is concentrated using either pepsin or trypsin. The wall of the *T. gondii* tissue cyst is ruptured during trypsin or pepsin digestion, releasing hundreds of bradyzoites. *T. gondii* tissue cysts are present, however it is impractical to identify them directly by microscopic analysis. Consequently, mice are used for bioassay of the digested substance. Prior to the detection of *T. gondii* infection, the mice that were infected with digested material had to be maintained for a duration of 6–8 weeks. Drinking cow's milk has little risk of contracting *T. gondii* infection since it is often pasteurized or boiled; however, drinking raw goat milk has been linked to infection [61-62].

- **HUMANS**

60% of children aged 6 to 8 in some parts of Brazil have antibodies to *T. gondii*, which is associated with consuming oocysts from an environment highly polluted with *T. gondii* oocysts [63-64]. The French practice of consuming some animal items raw or undercooked may have contributed to the high frequency of *T. gondii* infection in people in that country. However, large levels of oocyst contamination of the environment are likely the cause of the high incidence of *T. gondii* infection throughout Central and South America [65]. It is unusual for sexual activity, including kissing, to transmit disease. Blood transfusions and organ transplants are two further ways that *T. gondii* can spread: (i) when an organ or bone marrow from an infected donor is inserted into a non-immune, immunocompromised recipient; and (ii) when an immunocompromised, latently infected recipient contracts the illness. The cause of the infection is most likely tissue cysts in the donated tissue or in the latently infected transplant recipient [66-68]. *T. gondii* antibody detection in patients may help with diagnosis.

J) DIAGNOSIS

- The following serological techniques are available for the detection of humoral antibodies:
- The dye test of Sabin-Feldman,
- The tests include the latex agglutination test (LAT),
- The indirect hemagglutination assay,
- The indirect fluorescent antibody assay (IFA),
- The direct agglutination test, the enzyme-linked immunosorbent assay (ELISA), and

- The immunosorbent agglutination assay test (IAAT). [69-70].

The ideal scenario is to take two samples from the same person, the second being taken 2-4 weeks following the first. An acute infection is indicated by a 16-fold greater antibody titer in the second sample. Clinically speaking, determining the timing of an infection during pregnancy is crucial for medical action aimed at reducing fetal harm [71-73]. By inoculating laboratory animals and tissue cultures with secretions, excretions, bodily fluids, biopsy samples, and tissues with macroscopic lesions obtained after death, *Toxoplasma gondii* can be isolated from patients. Using the B1 gene as the target sequence, recent research has demonstrated that monoplex and multiplex PCR can be helpful in precisely identifying *T. gondii* from tissue biopsies, cerebral fluid, vitreous body from patients with undetected uveitis, foetal blood, and amniotic fluid [74-75]. Finding *T. gondii* in host tissue taken by biopsy or during a necropsy can be used to make the diagnosis. A quick diagnosis can be obtained by looking at impression smears of lesions under a microscope. The smears are fixed in methyl alcohol then dyed with one of the Romanowsky strains after drying for ten to thirty minutes. Sections of well-preserved *T. gondii* have a crescent shape, and the tachyzoites have an oval to spherical appearance. Tachyzoites of *T. gondii* are always found in vacuoles. The walls of tissue cysts can be stained with silver stain, and they are typically spherical in shape without septa. Bradyzoites have a high positive response when stained with periodic acid Schiff (PAS) [76].

K) TREATMENT STRATEGY

Medications such as pyrimethamine (Daraprim) and sulphadiazine are frequently used to treat toxoplasmosis. Sulphonamides, such as atovaquone, spiramycin, clindamycin, and diaminodiphenylsulphone, have been shown to inhibit the formation of tissue cysts in mice. Since soap and water destroy *T. gondii* in meat, all cutting boards, sink tops, knives, and everything coming into touch with raw meat should be cleaned with it [77]. *Toxoplasma* in tissue cysts can also be eliminated by gamma radiation exposure of 0.5 kilorads. Any animal's meat should be cooked to a temperature of 67°C. Pregnant ladies should stay away from raw meat, dirt, and cats. Meals for pet cats should only be prepared, tinned, or dried. In conclusion, people are frequently infected with the protozoan parasite *T. gondii*. In immune-competent people, it results in an infection with no symptoms. All meat should be thoroughly cooked before consumption in order to prevent human illness. To avoid exposure to soil infected with *T. gondii*, children should wear gloves when gardening and cover their sandboxes when not in use [78].

L) INFECTIONS ARE ASSOCIATED WITH COSTLY BOLDNESS TOWARD FELIDS IN A WILD HOST

Costly behavior toward *T. gondii*'s definitive hosts is linked to infections with the parasite in non-feline hosts. Hyena pups infected with *T. gondii* approach lions more closely than their uninfected counterparts, and their rates of lion fatality are greater, according to thirty years of field studies. One notorious instance of purported parasitic host manipulation is *Toxoplasma gondii*. Ingestion of *T. gondii* oocysts excreted from felids, ingestion of contaminated tissue from intermediate hosts, and birth-related infections are three ways that parasites might spread [79]. A wide range of warm-blooded hosts, illnesses are associated with a decreased aversion to or attraction to the smell of cat pee. It is believed that the effects of natural selection on the parasite led to the evolution of its capacity to modify host reactions to indirect signs of feline presence, hence increasing trophic transmission. In addition, *T. gondii* produces behavioral boldness and other potentially manipulative behaviors in intermediate hosts. This same boldness may encourage trophic transmission of *T. gondii* at the expense of intermediary hosts' fitness in the natural world if it leads to deadly interaction with felines. Significant disease load is also caused by *T. gondii* in human hosts. A limited corpus of natural research indicates that *T. gondii* coevolves with intermediates and definitive hosts, and that host fitness may be lowered by infection-related behavior [80].

II. CONCLUSION

The *T. gondii* infection is linked to a bold conduct that puts the infected hosts closer to animals, indicating that knowledgeable people may be better able to recognize hazards and discourage dangerous behavior. Natural selection on *T. gondii* has produced features that allow transmission from a variety of intermediary hosts into definitive hosts. Controlling audacity in a variety of hosts may be useful in biodiverse environments like as the Mara. A higher number of hosts can be infected across longer time and geographical scales by propagation from final hosts. Compared to asexual stage propagation, *T. gondii* may spread from an infected hyena to a lion through blood and tissue changes that occur during deadly confrontations, allowing the parasite to reproduce sexual. Furthermore, as hyena corpses are eaten by extremely mobile carrion-feeding animals that may disseminate the parasite far, a lion's killing of an infected hyena may further boost parasite transmission.

Despite being dead-end hosts, persons with *T. gondii* infection display riskier behavior. Findings showing that *T. gondii* infections in both human and non-human hosts equally modify homologous neuronal and hormonal regulators of behavior provide more evidence in favor of this theory. In the area of the host's downstream neuroendocrine alterations, significant advancements have been made. Parasites have a strong impact on host behavior, particularly when it comes to sexually chosen features and predator defense. Therefore, the sciences of neuroscience, behavioral ecology, and evolutionary biology stand to gain much from the clarification of *T. gondii*'s behavioral biology.

REFERENCES

- [1] Dubey J P, Beattie C P. Toxoplasmosis of animals and man. Boca raton, FLCRC press; 1988: 1-220
- [2] Dubey JP, Frenkel JK. Feline toxoplasmosis from acutely infected mice and the development of *Toxoplasma* cysts. J Protozool. 1976;23:537-546
- [3] Dubey JP, Lunney JK, Shen SK, Kwok OCH, Ashford DA, Thulliez P. Infectivity of low numbers of *Toxoplasma gondii* oocysts to pigs. J Parasitol. 1996;85:89-98
- [4] Freyre A, Dubey JP, Smith DD, Frenkel JK. Oocyst-induced *Toxoplasma gondii* infections in cats. J Parasitol. 1989;75:750-755
- [5] Dubey JP, Frenkel JK. Experimental *Toxoplasma* infection in mice with strains producing oocysts. J Parasitol. 1973;59:505-512
- [6] Dubey JP, Speer CA, Shen SK, Kwok OCH, Blixt JA. Oocyst-induced murine toxoplasmosis life cycle, pathogenicity and stage conversion in mice fed *Toxoplasma gondii* oocysts. J Parasitol. 1997;83:870-882
- [7] Speer CA, Dubey JP. Ultrastructure of early stages of infections in mice fed *Toxoplasma gondii* oocysts. Parasitology. 1998; 116:35-42
- [8] Dubey JP. Bradyzoite induced murine toxoplasmosis stage conversion, pathogenesis, and tissue cyst formation in mice fed bradyzoites of different strains of *Toxoplasma gondii*. J Euk Microbial. 1997;63:1121-24
- [9] Jacobs L, Remington JS, Melton ML. The resistance of the encysted form of *Toxoplasma gondii*. J Parasitol. 1960;46: 11-21
- [10] Dubey JP. Re-examination of resistance of *Toxoplasma gondii* tachyzoites and bradyzoites to pepsin and trypsin digestion. Parasitology; 1998: 43-50
- [11] Riemann HP, Meyer ME, Theis JH, Kelso G, Behymer DE. Toxoplasmosis in an infant fed unpasteurized goat milk. JPediatr. 1975;87:573-576
- [12] Dubey JP. Tissue cyst tropism in *Toxoplasma gondii*: a comparison of tissue cyst formation in organs of cats, and rodents fed oocysts. Parasitology. 1997;115:15-20
- [13] Bohne W, Gross U, Ferguson DJP, Heesemann J. Cloning and characterization of a bradyzoites specifically expressed gene of *Toxoplasma gondii*, related to genes encoding small heat shock proteins of plants. Molecular Microbiology. 1995;87:573-576
- [14] Halonen SK, Lyman WD, Chiu FC. Growth and development of *Toxoplasma gondii* in human neurons and astrocytes. J Neuropathol Exp Neurol. 1996;82:340-370
- [15] Weiss LM, Laplace D, Takvorian PM, Tanowitz HB, Cali A, Wittner MA. Cell culture system for study of the development of *Toxoplasma gondii* bradyzoites. J Euk Microbiol. 1995; 42: 150-157
- [16] Salm M, Fischer HG, Gross U, Reiter-Owona I, Seitz HM. Cyst formation by *Toxoplasma gondii* in vivo and in brain cell culture: a comparative morphology and immunocytochemistry study. Parasitol Res. 1996;75:75-86
- [17] Speer CA, Tilley M, Temple ME, Blixt JA, Dubey JP, White MW. Sporozoites of *Toxoplasma gondii* lack dense granule protein GRA2 and form a unique parasitophorous vacuole. Mol Biochem Parasitol. 1995;75:75-86
- [18] Flegr J, Prandota J, Sovičková M, Israili ZH. Toxoplasmosis-a global threat. Correlation of latent toxoplasmosis with specific disease burden in a set of 88 countries. PLoS ONE. 2014;9:e90203
- [19] Jones JL, Parise ME, Fiore AE. Neglected parasitic infections in the United States: toxoplasmosis. Am J Trop Med Hyg. 2014; 90:794-99.
- [20] Berdoy M, Webster JP, Macdonald DW. Fatal attraction in rats infected with *Toxoplasma gondii*. Proc Biol Sci. 2000; 267:1591-94.
- [21] Vyas A, Kim SK, Giacomini N, Boothroyd JC, Sapolsky RM. Behavioral changes induced by *Toxoplasma* infection of rodents are highly specific to aversion of cat odors. Proc Natl Acad Sci USA. 2007;104:6442-47.
- [22] Tyebji S, Seizova S, Hannan AJ, Tonkin CJ. Toxoplasmosis: A pathway to neuropsychiatric disorders. Neurosci Biobehav Rev. 2019;96:72-92
- [23] Worth AR, Andrew Thompson RC, Lymbery AJ. Reevaluating the evidence for *Toxoplasma gondii*-induced behavioural changes in rodents. Adv Parasitol. 2014;85:109-42.

- [24] Lamberton PH, Donnelly CA, Webster JP. Specificity of the *Toxoplasma gondii*-altered behaviour to definitive versus non-definitive host predation risk. *Parasitology*. 2008;135:1143–50.
- [25] Berdoy M, Webster JP, Macdonald DW. Parasite-altered behaviour is the effect of *Toxoplasma gondii* on *Rattus norvegicus* specific? *Parasitology*. 1995;111(Pt 4):403–9.
- [26] Afonso C, Paixão VB, Costa RM. Chronic *Toxoplasma* infection modifies the structure and the risk of host behavior. *PLoS ONE*. 2012;7:e32489
- [27] Boillat M, Hammoudi PM, Dogga SK, Pagès S, Goubiran M, Rodriguez I. Neuroinflammation-associated specific manipulation of mouse predator fear by *Toxoplasma gondii*. *Cell Rep*. 2020;30(320–34):e6
- [28] Saeij JP, Boyle JP, Boothroyd JC. Differences among the three major strains of *Toxoplasma gondii* and their specific interactions with the infected host. *Trends Parasitol*. 2005;21:476–81.
- [29] Ingram WM, Goodrich LM, Robey EA, Eisen MB. Mice infected with lowvirulence strains of *Toxoplasma gondii* lose their innate aversion to cat urine, even after extensive parasite clearance. *PLoS One*. 2013;8:e75246.
- [30] Hamilton WD, Zuk M. Heritable true fitness and bright birds: a role for parasites? *Science*. 1982;218:384–87.
- [31] Dawkins R. *The extended phenotype*, Vol. 8. Oxford: Oxford University Press; 1982.
- [32] Tong WH, Abdulai-Saiku S, Vyas A. Medial amygdala arginine vasopressin neurons regulate innate aversion to cat odors in male mice. *Neuroendocrinology*. 2020
- [33] Sutherland AL, Fond G, Kuin A, Koeter MW, Lutter R, Van Gool T. Beyond the association. *Toxoplasma gondii* in schizophrenia, bipolar disorder, and addiction: systematic review and meta-analysis. *Acta Psychiatr Scand*. 2015;132:161–79.
- [34] Xiao J, Prandovszky E, Kannan G, Pletnikov MV, Dickerson F, Severance EG *Toxoplasma gondii*: biological parameters of the connection to schizophrenia. *Schizophr Bull*. 2018;44:983–92.
- [35] Buck JC, Ripple WJ. Infectious agents trigger trophic cascades. *Trends EcolEvol*. 2017;32:681–94.
- [36] Lim A, Kumar V, Hari Dass SA, Vyas A. *Toxoplasma gondii* infection enhances testicular steroidogenesis in rats. *Mol Ecol*. 2013;22:102–10.
- [37] Gaskell EA, Smith JE, Pinney JW, Westhead DR, McConkey GA. A unique dual activity amino acid hydroxylase in *Toxoplasma gondii*. *PLoS One*. 2009;4:e4801.
- [38] Martin HL, Alsaady I, Howell G, Prandovszky E, Peers C, Robinson P. Effect of parasitic infection on dopamine biosynthesis in dopaminergic cells. *Neuroscience*. 2015;306:50–62.
- [39] Prandovszky E, Gaskell E, Martin H, Dubey JP, Webster JP, McConkey GA. The neurotropic parasite *Toxoplasma gondii* increases dopamine metabolism. *PLoS One*. 2011;6:e23866
- [40] Hari Dass SA, Vyas A. *Toxoplasma gondii* infection reduces predator aversion in rats through epigenetic modulation in the host medial amygdala. *Mol Ecol*. 2014;23:6114–22.
- [41] Dubey JP. Advances in the life cycle of *Toxoplasma gondii*. *Int J Parasitol*. 1998;28:1019–24.
- [42] Michalakis Y, Hochberg ME. Parasitic effects on host life-history traits: a review of recent studies. *Parasite*. 1994;1:291–94
- [43] Jones ME, Cockburn A, Hamede R, Hawkins C, Hesterman H, Lachish S. Life-history change in disease-ravaged Tasmanian devil populations. *Proc Natl Acad Sci USA*. 2008;105:10023–7.
- [44] Dubey JP, Beattie CP. *Toxoplasmosis of Animals and Man*. Boca Raton, FL: CRC Press, 1988
- [45] Desmonts G, Couvreur J. Congenital toxoplasmosis. A prospective study of 378 pregnancies. *N Engl J Med* 1974; 290: 1110–16.
- [46] Remington JS, McLeod R, Desmonts G. Toxoplasmosis. In: Remington JS, Klein JO, eds. *Infectious Disease of the Fetus and Newborn Infant*. Philadelphia: W.B. Saunders Company, 1995; 140–267.
- [47] Roberts T, Frenkel JK. Estimating income losses and other preventable costs caused by congenital toxoplasmosis in people in the United States. *J Am Vet Med Assoc* 1990; 196: 249–56.
- [48] Roberts T, Murrell KD, Marks S. Economic losses caused by foodborne parasitic diseases. *Parasitol Today*. 1994; 10: 419–23.
- [49] Benenson MW, Takafuji ET, Lemon SM et al. Oocyst-transmitted toxoplasmosis associated with ingestion of contaminated water. *N Engl J Med* 1982; 307: 666–69.
- [50] Bowie WR, King AS, Werker DH et al. Outbreak of toxoplasmosis associated with municipal drinking water. *Lancet*. 1997; 350: 173–77.
- [51] Teutsch SM, Juranek DD, Sulzer A. Epidemic toxoplasmosis associated with infected cats. *N Engl J Med*. 1979; 300: 695–99.
- [52] Burnett AJ, ShorttSG, Isaac-Renton J, King A, Werker D, Bowie WR. Multiple cases of acquired toxoplasmosis retinitis presenting in an outbreak. *Ophthalmology* 1998; 105: 1032–37
- [53] Smith JL. Documented outbreaks of Toxoplasmosis: Transmission of *Toxoplasma gondii* to humans. *J Food Prot* 1993; 56: 630-39.

- [54] Luft BJ, Remington JS. Toxoplasmic encephalitis in AIDS. Clin Infect Dis 1992; 15: 211–22.
- [55] Dubey JP. Oocyst shedding by cats fed isolated bradyzoites and comparison of infectivity of bradyzoites of the VEG strain *Toxoplasma gondii* to cats and mice. J Parasitol. 2001; 87: 215–9.
- [56] Bahia-Oliveira LMG, Wilken de Abreu AM, Azevedo-Silva J. Toxoplasmosis in southeastern Brazil: an alarming situation of highly endemic acquired and congenital infection. Int J Parasitol. 2001; 31: 133–6.
- [57] Cole RA, Lindsay DS, Howe DK et al. Biological and molecular characterizations of *Toxoplasma gondii* strains obtained from southern sea otters (*Enhydra lutris nereis*). J Parasitol. 2000; 86: 526–30.
- [58] Dubey JP, Odening K. Toxoplasmosis and related infections in Parasitic Diseases of Wild Mammals. Ames, IA: Iowa State University Press. 001; 478: 5190.
- [59] Dubey JP, Weigel RM, Siegel AM. Sources and reservoirs of *Toxoplasma gondii* infection on 47 swine farms in Illinois. J Parasitol. 1995; 81: 723–29.
- [60] Warnekulasuriya MR, Johnson JD, Holliman RE. Detection of *Toxoplasma gondii* in cured meats. Int J Food Microbiol. 1998; 45: 211–15.
- [61] Jauregue LH, Higgins JA, Zarlenga DS et al. Development of a real-time PCR assay for the detection of *Toxoplasma gondii* in pig and mouse tissues. J Clin Microbiol 2001; 39: 2065–71.
- [62] Frenkel JK. The Coccidia. Eimeria. Isospora, Toxoplasma and Related Genera. Toxoplasmosis: Parasite Life Cycle, Pathology and Immunology. Baltimore, MD: University Park Press, 1973; 343–410.
- [63] Burg JL, Grover CM, Pouletty P, Boothroyd JC. Direct and sensitive detection of a pathogenic protozoan, *Toxoplasma gondii*, by polymerase chain reaction. J Clin Microbiol. 1989; 8: 1787–92.
- [64] Julander I, Martin C, Lappalainen M. Polymerase chain reaction for diagnosis of cerebral toxoplasmosis in cerebral fluid in HIV-positive patients. Scand J Infect Dis 2001; 33: 538–41.
- [65] Guerina NG, Hsu HW, Meissner HC. Neonatal serologic screening and early treatment for congenital *Toxoplasma gondii* infection. The New England Regional Toxoplasma Working Group. N Engl J Med. 1994; 330: 1858–63.
- [66] Dubey JP, Thayer DW. Killing of different strains of *Toxoplasma gondii* tissue cysts by irradiation under defined conditions. J Parasitol. 1994; 80: 764–67.
- [67] Poulin, R. Parasite Manipulation of Host Behavior: An Update and Frequently Asked Questions. Advances in the Study of Behavior 41, (Elsevier Inc., 2010)
- [68] Dubey, J. Advances in the life cycle of *Toxoplasma gondii*. Int. J. Parasitol. 1998. 28: 1019–1024.
- [69] Elmore, S. A. *Toxoplasma gondii*: epidemiology, feline clinical aspects, and prevention. Trends Parasitol. 2010; 26: 190–196.
- [70] Flegr, J., Lenochová, P., Hodný, Z. & Vondrová, M. Fatal attraction phenomenon in humans—cat odour attractiveness increased for *Toxoplasma* infected men while decreased for infected women. PLoSNegl. 2005. Trop. Dis; 5: e1389.
- [71] Vyas, A., Kim, S.-K., Giacomini, N., Boothroyd, J. C. & Sapolsky, R. M. Behavioral changes induced by *Toxoplasma* infection of rodents are highly specific to aversion of cat odors. Proc. Natl Acad. Sci. USA. 2007; 104: 6442–47.
- [72] Di Genova, B. M., Wilson, S. K., Dubey, J. P. & Knoll, L. J. Intestinal delta-6- desaturase activity determines host range for *Toxoplasma* sexual reproduction. PLoSBiol 2019; 17: 1–19.
- [73] Boillat, M. Neuroinflammation-associated specific manipulation of mouse predator fear by *Toxoplasma gondii*. Cell Rep. 2020; 30: 320–334
- [74] Webster, J. P. The effect of *Toxoplasma gondii* on animal behavior: playing cat and mouse. Schizophr. Bull. 2007; 33: 752–756.
- [75] Tenter, A. M., Heckeroth, A. R. & Weiss, L. M. *Toxoplasma gondii*: from animals to humans. Int. J. Parasitol. 2000; 30: 1217–58.
- [76] Worth, A. R., Lymbery, A. J. & Thompson, R. C. A. Adaptive host manipulation by *Toxoplasma gondii*: fact or fiction? Trends Parasitol. 2013; 29: 150–155
- [77] Shapiro, K. et al. Type X strains of *Toxoplasma gondii* are virulent for southern sea otters (*Enhydra lutris nereis*) and present in felids from nearby watersheds. Proc. R. Soc. B Biol. Sci. 2019; 286: 1–10.
- [78] Siegel, S. E. et al. Transmission of toxoplasmosis by leukocyte transfusion. 1971; 37: 388–94.
- [79] Jones, S., Strauss, E. & Holekamp, K. Ecology of African carrion. In Carrion ecology, evolution, and their applications (eds. Benbow, M., Tomberlin, J. & Tarone, A.) 461–491 (CRC Press, 2015)
- [80] Webster, J. P. & Mc Conkey G. A. *Toxoplasma gondii*-altered host behaviour: Clues as to mechanism of action. Folia Parasitol Praha. 2010; 57: 95–104.



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