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Schizophrenia: The Dark Side of Toxoplasmosis

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Dear Editor,

Toxoplasma gondii is an intracellular parasite that has been associated with several mental disorders. It usually causes an inapparent primary infection. Found worldwide, *T. gondii* is capable of infecting virtually all warm-blooded animals.[1-3]

Schizophrenia is a neurological disorder characterized with long-term and devastating neuropsychological problems, usually presenting in adolescents or young adults. The disease affects almost 1.1% of the global population including all races and ethnic groups with an equal prevalence in both sexes.[1] *T. gondii* seroprevalence is strongly associated with 12-month generalized anxiety disorder but not with other anxiety, depressive, or alcohol-related disorders. Because of the intracellular nature of some parasites, their treatment and development of new drugs is a major challenge for scientists.[4] Recently, the use of nanoparticles and nano-scaffolds has suggested for the treatment of parasitic diseases, although limited research has been done in this regard.[5-7]

Toxoplasma gondii modulates the secretion of neurotransmitters (such as dopamine) via producing tyrosine hydroxylase and interacting with astrocyte glial cells. Therefore, this parasite can be related to the pathogenesis of schizophrenia. The association between schizophrenia and toxoplasmosis requires researchers to investigate links between this parasitic infection with other neurological disorders such as paranoia, depression, and brain injuries. A higher probability of schizophrenia has been recorded in those who have antibodies against *T. gondii* in their sera. It has been suggested that *T. gondii* is translocated to target cerebral regions via dendritic cells and macrophages.[1]

The parasite cysts have been identified in astrocytes, indicating possible interactions between *T. gondii* cysts and these cells. In the brain tissue experimentally infected with virulent type I *T. gondii,* parasites were shown to be localized around neuronal nuclei of astrocytes. Therefore, research evidence suggests that *T. gondii* can play the role of a neuromodulator and infect neuronal cells within the brain.[1]

In fact, *T. gondii* cysts have been detected in various cerebral regions including basal ganglia, olfactory bulbs, hippocampus, thalamus, diencephalon, cortex, as well as in the amygdale, further highlighting the possible role of this parasite in brain damages.[1] It has been suggested that *T. gondii* may use genes to augment its survival in its intermediate and definitive hosts. For reaching this goal, these genes may facilitate the translocation of the parasite to the brain to promote required behavioral modifications.[1]

The main aim of using nanoparticles/nano-scaffolds is to use them as a drug delivery system and to release the drug agent to affect the specific site. Recently, the use of particle systems such as nanomedicine has been advocated as a physical tool to improve the pharmacokinetic properties of various types of drug molecules *in vivo*.[5-8]

Another point supporting a link between schizophrenia and *T. gondii* is that both of these conditions can modulate the brain at early developmental stages. It has been noted that disorders such as schizophrenia, sclerosis, and Parkinson's disease originate at early phases of the brain development. On the other hand, *T. gondii* is also able to infect the brain even in the perinatal period.[1]

A link has been proposed between *T. gondii* infection and the onset and progression of schizophrenia and other bipolar disorders. A study showed that *T. gondii* can infect the brain by creating cysts within its neurons and by producing tyrosine hydroxylase, an enzyme required for dopamine production.[1]

Dopamine regulates sleep cycle, motivation, attention, mood, and social activities. Also, a link between

dopamine and schizophrenia is well characterized, and all the drugs used to treat schizophrenia target this neurotransmitter. The levels of some neurotransmitters including dopamine (along with norepinephrine, etc) are affected in the patients infected with *T. gondii* as well; a process which is also known to be part of schizophrenia pathogenesis.[1] Dopamine is important in regulating perceptional, behavioral, and other functional properties of the brain. Elevated levels of dopamine are related to the pathogenesis of a variety of neurological disorders such as schizophrenia and mania. For this reason, many drugs used to treat neuronal disorders target dopamine in part of their action.[1]

Multiple studies have been conducted in various populations to divulge the association between schizophrenia and *T. gondii* infection. Overall, these studies suggest a significant association between schizophrenia and toxoplasmosis, which can be the basis for opening a new path for treating psychiatric and neuronal diseases.[1]

Conflict of Interest

The authors declare that they have no conflict of interests.

Ethical Statement

Not applicable.

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