Assessing the Relationship Between Exposure to Toxoplasma gondii and the Development of Schizophrenia: Is There Really Something Up with Cat People?

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Abstract

Background: Multiple studies have proposed a relationship between infection with the parasite Toxoplasma gondii (T. gondii) and the onset of schizophrenia. Humans are infected with this parasite via exposure to cat feces, ingesting contaminated food and water or through transplacental transmission. It is estimated that roughly 11% of the world population is infected with Toxoplasma. Schizophrenia is a psychiatric disorder, and affects approximately 1.1% of the population over 18 years old worldwide. We hypothesize that individuals infected with Toxoplasma may be at an increased risk of developing schizophrenia.

Objective/Purpose: To elucidate the relationship between exposure to Toxoplasma gondii and the development of schizophrenia.

Methods: Journals such as Nature, Annals of General Psychiatry, The Journal of Psychoses and Related Disorders, Acta PsychiatricaScandinavica, Infectious Diseases Society of America, Schizophrenia Research and The U.S. National Library of Medicine National Institutes of Health were used to collect information regarding exposure to T. gondii and the development of schizophrenia. Limits of our search involved language and the onset of schizophrenia.

Results: 9 relevant studies were found. The type of reviews and study designs varied, including 2 meta-analyses, 4 case controls, 1 cross sectional analysis, 1 prospective cohort study and 1 narrative review. 8 of the 9 studies reported statistically significant data showing increased levels of T. gondii in schizophrenic patients. P-values, chi-square, and odds ratio measures of association were used to determine statistical significance.

Conclusion: There is a growing body of data to indicate that T. gondii infection may be associated with the development of schizophrenia. Further study is needed to determine a concrete association between T. gondii infection and schizophrenia, as well as to elucidate the mechanism relating infection with T. gondii to the development of schizophrenia.

Background

Toxoplasma gondii is a prevalent neurotropic parasite; 11% of world population¹
• In developing regions, it is estimated that 95% of the population may be infected with the parasite
• T. gondii is transmitted through poor food and water, congenitally and cat feces² (Figure 1)

Schizophrenia is a psychiatric disorder of unknown etiology, and affects approximately 1.1% of the world’s population over 18 years old²
• It is proposed that genetic, as well as environmental factors may influence the onset of schizophrenia

• Increased levels of antibodies to neurotropic pathogens are found in multiple mental illnesses
• It has been postulated that T. gondii may confer a substantial risk to the development of schizophrenia

• Levels are measured by antibody titre

Many studies have proposed a relationship between infection with the parasite Toxoplasma gondii (T. gondii) and the onset of schizophrenia.

Research Question

Are individuals who are infected with Toxoplasma gondii at a significantly increased risk of developing schizophrenia?

Methods

Structured Literature Review (Figure 2)

Inclusion Criteria
• Humans
• Schizophrenia
• Articles
• English
• Non-articles sources

Exclusion Criteria
• Humans
• Schizophrenia

Results

Table 1. Summary of findings from literature review

Reference

TI= 758
T. gondii has high affinity for brain tissue and also cytoxys (amy.
Two infection is associated with early brain development leading to disease pathogenesis
Higher exposure to cat in childhood among those with schizophrenia
T. gondii has infected levels of IgM in bra (irrespective of schizophrenia
T. gondii should be considered in the etiological pathway for schizophrenia

Methods

Statistically significant differences were found between case and control groups

References

References

Nelson, M.H., Alameen, M. and Baker, P., 2010. A meta-review in schizophrenia; however, etiology remains uncertain

Berkson’s bias

No RCT: ethical limitations

Discussion

• All articles supported the relationship

• Substantial evidence linked infection with T. gondii to the development of schizophrenia

• Molecular evidence (i.e. affinity to brain tissue, antibody levels)

• Cumulative effects (Hubel et al., 2013)

• Statistically significant findings

• All studies involving antibodies (1/1) found that the prevalence of antibodies to T. gondii in individuals with schizophrenia is significantly higher than the prevalence of antibodies in control populations

• Statistical power in studies is not based on the direct detection

• Satisfactory evidence is provided which elucidates the pathophysiology and mechanism by which T. gondii contributes to the development of schizophrenia

• May lead to novel treatments/new understanding of schizophrenia or other related disorder

• Schizophrenia has not been found to be unusually prevalent in these countries

• Several studies measured antibody levels subsequent to diagnosis

• Future research should focus on the timing of the infection

• No indication that schizophrenia incidence is narrowly linked to endemic variations in T. gondii infections

• Not everyone with schizophrenia can be diagnosed/identified

• Many causes of schizophrenia are hypothesized including a likely genetic component³

• Bradford Hill Criteria

• Strength

• Temporality

• Biological gradient

• Coherence

• Experiment

• Specificity

• Plausibility

• There may be a latent period between initial infection and experience of symptoms making it difficult to prove causality³

• T. gondii is highly prevalent in the general population³

• The diagnostic criteria for schizophrenia used in the United States (Diagnostic and Statistical Manual of Mental Disorders), Europe (International Classification of Diseases), and China (Classification and Diagnostic Standards of Mental Disorders in China) are very similar

• Undefined patient populations: in several studies the patient selection and how the patients were enrolled is not indicated

• Mortensen et al., (2007) focused on early onset schizophrenia (18 under)

• Association between schizophrenia and T. gondii reflects an underlying noncausal association schizophrenia and the exposure to T. gondii rather than a causal association

• Non-disclosure of patient selection criteria

• Bias

• Reporting

• Foreign exclusion bias

• Ease of access

Conclusion

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• Plausibility

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• No indication that schizophrenia incidence is narrowly linked to endemic variations in T. gondii infections

• Further study is needed to ascertain the relationship between T. gondii and the outcome of schizophrenia

• A double-blind randomized control trial would produce the most conclusive results however due to ethical issues it is unlikely this will occur

References

1. NIMH. (2017). Schizophrenia; however, etiology remains uncertain


3. No indication that schizophrenia incidence is narrowly linked to endemic variations in T. gondii infections

4. Not everyone with schizophrenia can be diagnosed/identified

5. Many causes of schizophrenia are hypothesized including a likely genetic component

6. Bradford Hill Criteria

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20. A double-blind randomized control trial would produce the most conclusive results however due to ethical issues it is unlikely this will occur