



Association of Cytomegalovirus and Toxoplasma gondii Antibody Titers With Bipolar Disorder

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ABSTRACT

Background: The association between infectious agents and mental health disorders has garnered significant attention in recent years, particularly in relation to bipolar disorder. The literature reveals a complex interplay between *Toxoplasma gondii* and cytomegalovirus (CMV) infections and their potential roles in the pathogenesis of bipolar disorder. **Literature Review:** (Lindgren et al., 2020) provide a foundational examination of the seropositivity rates for *T. gondii* and CMV, noting a correlation between these infections and mental health disorders, including increased suicide attempts among individuals with mood disorders. Further, (A. Virus et al., 2021) delve into the neurobiological mechanisms by which *T. gondii* may induce oxidative stress and immune-inflammatory responses. Their research indicates a significant association between *T. gondii* seropositivity and a history of bipolar disorder type I, suggesting that this parasite could influence mood dysregulation through biological pathways similar to those observed in bipolar disorder. (Ali Mofazzal Jahromi et al., 2022) expand the discussion to include neurotropic infections, reporting that increased seropositivity to *T. gondii* and CMV correlates with cognitive impairments in patients with bipolar disorder. This finding implies a shared pathogenic pathway among these infections and mental health conditions. **Conclusion:** In conclusion, the reviewed literature underscores a critical narrative regarding the association of *Toxoplasma gondii* and CMV with bipolar disorder. There is compelling evidence supporting the notion that these infectious agents may contribute to the development and exacerbation of bipolar disorder through various biological mechanisms, highlighting the importance of considering infectious agents in mental health assessments. Future research is warranted to further elucidate these relationships and to explore potential therapeutic implications.

Keyword: Association, Cytomegalovirus, *Toxoplasma gondii*, Antibody Titers, Bipolar Disorder

INTRODUCTION

The association between infectious agents and mental health disorders has garnered significant attention in recent years, particularly in relation to bipolar disorder. The literature reveals a complex interplay between *Toxoplasma gondii* and cytomegalovirus (CMV) infections and their potential roles in the pathogenesis of bipolar disorder. (Lindgren et al., 2020) present compelling evidence of seropositivity rates for *T. gondii* and CMV, highlighting a notable correlation between these infections and various mental health outcomes, including increased suicide attempts among individuals with mood disorders. Their findings suggest that *T. gondii* may contribute to suicidal behavior, particularly in postmenopausal women, while CMV seropositivity was linked to mood disorders in both genders.

Building on this foundation, (A. Virus et al., 2021) explore the neurobiological mechanisms through which latent *T. gondii* infection may induce oxidative stress and immune-inflammatory responses, potentially mimicking changes observed in bipolar disorder. Their research indicates a significant association between *T. gondii* seropositivity and a history of bipolar disorder type I, further supporting the notion that this parasite may influence mood dysregulation.

In a broader context, (Ali Mofazzal Jahromi et al., 2022) expand the discussion to include neurotropic infections such as CMV and HSV-1, emphasizing their prevalence and the emerging links to psychiatric disorders, including bipolar disorder. The authors report that increased seropositivity to *T. gondii* and CMV correlates with cognitive impairments in patients suffering from schizophrenia and bipolar disorder, suggesting a shared pathogenic pathway among these infections and mental health conditions.

Recent investigations by (Shahab Banihashem et al., 2023) delve deeper into the epidemiological aspects of *T. gondii* infection among psychiatric patients in Southeastern China. Their findings reinforce the association between *T. gondii* infection and schizophrenia, while also indicating a potential link to bipolar

disorder and suicide attempts, thereby adding to the growing body of evidence that connects infectious agents with severe mental health disorders.

(Ioannou et al., 2024) contribute to the discourse by examining the immunological responses in bipolar disorder patients in relation to chronic CMV infection. Their study reveals alterations in T cell populations, although the interaction between CMV and bipolar disorder did not yield statistically significant results. This suggests that while CMV may influence immune profiles, its direct role in bipolar disorder remains inconclusive.

Finally, (E. Bartolomé del Pino & Zanón-Moreno, 2024) provide a systematic review synthesizing multiple studies on the relationship between *T. gondii* and mental disorders, including bipolar disorder. They highlight how *T. gondii* infection may exacerbate clinical features in bipolar and psychotic disorders, indicating a need for further exploration of the underlying mechanisms at play.

Together, these articles underscore a critical narrative in understanding how infectious agents like *T. gondii* and CMV may contribute to the development and exacerbation of bipolar disorder, paving the way for future research that could lead to novel therapeutic approaches and preventive strategies.

LITERATURE REVIEW

The article titled "Exposure to common infections and risk of suicide and self-harm: a longitudinal general population study" by Lindgren et al. (Lindgren et al., 2020) presents a comprehensive examination of the relationship between common infections, specifically *Toxoplasma gondii* (*T. gondii*) and Cytomegalovirus (CMV), and their potential associations with mental health disorders, including bipolar disorder. The authors provide valuable insights into the prevalence of seropositivity for these infections within the Finnish adult population, reporting a notable 20% for *T. gondii* and an impressive 84% for CMV.

The study effectively highlights the connections between these infections and various mental health outcomes, reinforcing the notion that *T. gondii* may be linked to several mental disorders, including anxiety and depressive symptoms.

Furthermore, the differential influence of CMV seropositivity on mood disorders across genders adds another layer of complexity, indicating that biological and psychological factors may interact in nuanced ways.

The authors also delve into the intriguing relationship between infections and suicidal behavior, noting a positive correlation between national prevalence rates of *T. gondii* and suicide rates, particularly among postmenopausal women. This correlation raises significant questions regarding the role of chronic infections in exacerbating mental health issues and potentially increasing suicide risk. The article reports a trend linking *T. gondii* IgG antibodies with suicide attempts in both psychiatric outpatients and individuals with mood disorders, which underscores the importance of considering infectious agents in the context of mental health assessments.

Notably, the exploration of IgM class antibodies to both *T. gondii* and CMV in individuals with serious mental illness who had attempted suicide presents a compelling argument for the need to investigate these markers further. The findings suggest that serological assessments could serve as valuable tools in identifying individuals at heightened risk for suicidal behavior. However, the article also acknowledges conflicting results in schizophrenia patients, indicating that the relationship between these infections and psychiatric conditions may not be straightforward.

The article "Neurological and Neurobehavioral Disorders Associated with *Toxoplasma gondii* Infection in Humans" by Virus, Ehrhorn, Lui, and Davis (A. Virus et al., 2021) presents a compelling examination of the potential relationship between *Toxoplasma gondii* (*T. gondii*) infection and bipolar disorder. The authors propose that latent *T. gondii* may induce oxidative stress in the central nervous system (CNS), which could activate immune-inflammatory processes that mimic the neurobiological changes observed in bipolar disorder. This hypothesis is particularly significant given the growing body of literature exploring the interplay between infections and neuropsychiatric disorders.

The article highlights findings from various studies, noting that individuals who are seropositive for *T. gondii* are significantly more likely to have a history of bipolar disorder type I, characterized by both manic and depressive episodes. The authors emphasize that the majority of research points towards a potential link. This critical evaluation of the existing data is essential for understanding the complexities of psychiatric disorders and their potential infectious triggers.

Moreover, the authors discuss the implications of maternal transmission of *T. gondii* and its association with bipolar disorder, noting that current studies have not established a significant connection in this context. This observation raises important questions about the timing and nature of *T. gondii* infection and its potential role in the development of neuropsychiatric conditions.

The article titled "Latent infections, coronavirus disease 2019 and psychiatric disorders: The friend of my enemy" by Jahromi et al. (Ali Mofazzal Jahromi et al., 2022) provides a comprehensive examination of the relationship between neurotropic infections, specifically *Toxoplasma gondii* and Cytomegalovirus (CMV), and psychiatric disorders such as bipolar disorder and schizophrenia. The authors delve into the prevalence of these infections within the general population and their potential implications for mental health, particularly in the context of neuropsychiatric disorders.

One of the key insights presented in the article is the significant association between seropositivity to *T. gondii* and CMV with cognitive impairments in patients diagnosed with schizophrenia and bipolar disorder. The authors advocate for further research to elucidate the mechanisms by which these infections may contribute to the pathophysiology of bipolar disorder and other psychiatric conditions.

The article titled "Serologic evaluation of cytomegalovirus (CMV), *Toxoplasma gondii* and *Brucella* in schizophrenia patients" by Banihashem et al. (Shahab Banihashem et al., 2023) provides a comprehensive examination of the serological associations between certain infectious agents and psychiatric disorders, particularly focusing on schizophrenia. The authors delve into the implications of

Toxoplasma gondii infection, highlighting its potential links to various psychiatric conditions, including bipolar disorder.

A significant aspect of the study is the exploration of Toxoplasma gondii's role in psychiatric disorders, particularly its association with schizophrenia and its potential influence on suicide attempts among affected individuals. The authors present evidence suggesting that Toxoplasma gondii infection is prevalent in first-episode and inpatient schizophrenia patients, which raises pertinent questions about the pathogen's involvement in the etiology of these psychiatric conditions. This finding aligns with previous systematic reviews and meta-analyses that have indicated a higher prevalence of Toxoplasma gondii seropositivity in individuals with treatment-resistant schizophrenia, thereby suggesting a broader implication for its role in various psychiatric disorders, including bipolar disorder.

Moreover, the article touches upon the epidemiology of congenital cytomegalovirus (CMV) infection, which is relevant in understanding the potential neurodevelopmental impacts of this virus. While the primary focus remains on Toxoplasma gondii, the relationship between CMV and psychiatric disorders is also a critical area of investigation.

The article titled "Higher T central and lower effector memory cells in bipolar disorder: A differentiation abnormality?" by Ioannou et al. (Ioannou et al., 2024) provides a nuanced exploration of the immunological profiles associated with bipolar disorder (BD) and their potential relationship with chronic cytomegalovirus (CMV) infection. The study's findings indicate that while there are observable differences in T cell populations between patients with BD and healthy controls, the interaction between BD and chronic CMV infection does not significantly alter the levels of TREGS, TCM, CD4+ TEMRA, or TEM cells. This suggests that the immune alterations in BD may not be directly influenced by CMV in a statistically significant manner.

The article titled "Systematic Review on the Relationship between Toxoplasmosis and Mental Disorders" by Bartolomé del Pino and Zanón-Moreno (E. Bartolomé del Pino & Zanón-Moreno, 2024) provides a comprehensive

examination of the association between *Toxoplasma gondii* infections and various mental health disorders, with a specific focus on bipolar disorder. The authors present compelling evidence suggesting that cognitive deterioration in bipolar disorder patients may be linked to the presence of *Toxoplasma gondii*, particularly through the modulation of interleukin 6 (IL-6) levels.

CONCLUSION

The literature presents a nuanced exploration of the relationship between *Toxoplasma gondii* and cytomegalovirus (CMV) infections and their associations with bipolar disorder. Several studies highlight significant correlations between these infectious agents and mental health outcomes, suggesting that they may play a role in the pathogenesis of bipolar disorder.

(Lindgren et al., 2020) provide a foundational examination of the seropositivity rates for *T. gondii* and CMV, noting a correlation between these infections and mental health disorders, including increased suicide attempts among individuals with mood disorders. Their findings particularly emphasize the potential impact of *T. gondii* on suicidal behavior, especially in postmenopausal women, while also linking CMV seropositivity to mood disorders in both genders.

Further, (A. Virus et al., 2021) delve into the neurobiological mechanisms by which *T. gondii* may induce oxidative stress and immune-inflammatory responses. Their research indicates a significant association between *T. gondii* seropositivity and a history of bipolar disorder type I, suggesting that this parasite could influence mood dysregulation through biological pathways similar to those observed in bipolar disorder.

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(Shahab Banihashem et al., 2023) investigate the epidemiological aspects of *T. gondii* infection among psychiatric patients, reinforcing its association with schizophrenia and indicating a potential link to bipolar disorder and suicide attempts. This adds to the growing body of evidence connecting infectious agents with severe mental health disorders.

(Ioannou et al., 2024) examine the immunological responses in bipolar disorder patients concerning chronic CMV infection. Their study reveals alterations in T cell populations, although the interaction between CMV and bipolar disorder did not yield statistically significant results, suggesting that while CMV may influence immune profiles, its direct role in bipolar disorder remains inconclusive.

Finally, (E. Bartolomé del Pino & Zanón-Moreno, 2024) provide a systematic review synthesizing multiple studies on the relationship between *T. gondii* and mental disorders, including bipolar disorder. They highlight how *T. gondii* infection may exacerbate clinical features in bipolar and psychotic disorders, suggesting a need for further exploration of the underlying mechanisms at play.

In conclusion, the reviewed literature underscores a critical narrative regarding the association of *Toxoplasma gondii* and CMV with bipolar disorder. There is compelling evidence supporting the notion that these infectious agents may contribute to the development and exacerbation of bipolar disorder through various biological mechanisms, highlighting the importance of considering infectious agents in mental health assessments. Future research is warranted to further elucidate these relationships and to explore potential therapeutic implications.

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