TOXOPLASMOSIS AND SCHIZOPHRENIA PUBLICATION ACTIVITY IN 1991-2023: A WEB OF SCIENCE-BASED BIBLIOMETRIC ANALYSIS

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Abstract
Schizophrenia is a complicated mental condition marked by signs of psychosis, often leading to social and occupational decline. Schizophrenia has a complex etiology that is a result of the interplay between environmental factors (such as infectious illnesses) and a person's genetic disposition. Recent epidemiological research indicates that Toxoplasma gondii may cause schizophrenia. T. gondii-related studies in schizophrenia were the focus of this bibliometric analysis study. The Web of Science's electronic database was used to find T. gondii-related studies in schizophrenia. Co-authorship analyses of countries and keyword co-occurrence analyses were carried out using the VOSviewer software. In this bibliometric study, the research topic of T. gondii-related publications in schizophrenia during the last 33 years has been laid out, with the nations, organizations, authors, journals, main keywords, citations, and the top documents contributing to the basic knowledge structure. The significant increase in yearly publications implies that this research area has acquired importance on a global scale, with the United States having the most articles. The main organizations and researchers working on T. gondii studies on schizophrenia have been identified by this study. The outcomes give a thorough overview of this study field's terrain.

Keywords: Bibliometric analysis, schizophrenia, Toxoplasmosis, Toxoplasma gondii


INTRODUCTION
Infections caused by parasites are still prevalent in developing and laggard countries/regions, even though their prevalence is declining globally they can cause neurotropic involvements [1]. Toxoplasma gondii is a parasitic obligate intracellular protozoa, that relies on its hosts for survival [2]. The bulk of these infections are asymptomatic or result in a mild sickness similar to the flu during the time of acute infection in immunocompetent humans. The most symptomatic T. gondii condition affects immunocompromised people, such as Acquired Immune Deficiency Syndrome (AIDS)
patients or unborn fetuses, and is related to T. gondii's preference for and persistence in the brain [2].

Schizophrenia is a complicated mental condition marked by signs of psychosis, often leading to social and occupational decline. The etiology of this disorder is still controversial and continues to pose a challenge for its treatment [3,4]. Contrary to widespread assumption, men experience this disease slightly more frequently than women. Also, the results are not always negative. The symptoms of this disease are classified as follows: positive, negative, and disorganization syndromes. As catatonic symptoms are not solely regarded as schizophrenia, so-called first-order symptoms are no longer thought to be crucial for diagnosis. The condition now has cognitive impairment recognized as another clinical characteristic. Brain volume reductions of about 2% and lateral ventricular hypertrophy are well-established findings. Different frontal cortex subregions experience functional changes in the brain, which may eventually be explained by the disruption of interactions between broad neural networks [4].

Schizophrenia's etiology is multifaceted and involves the combination of environmental factors and genetic predisposition [5]. The possibility that a person may acquire the illness is influenced by environmental risk factors, such as difficulties during pregnancy and childbirth, traumatized childhood, forced migration, isolation from society, drug/substance/ alcohol abuse, and acting alone and in combination at different levels over time [5,6]. In addition to research on gene-environment interaction and environment-environment interaction, the establishment of a polygenic risk score for this disease has significantly improved the understanding of this disease [5]. According to recent epidemiologic studies, some schizophrenia cases may be caused by infectious diseases [7,8]. Perinatal infections, such as toxoplasmosis, syphilis, Rubella, Herpes Simplex Virus, and others cause neuropsychiatric disorders including mental retardation, difficulty with learning, sensorineural issues, and neuromorphological deficiencies [9].

Numerous lab research has demonstrated that T. gondii infection can impact behavior in immunocompetent animals. Various behavioral effects include a general decrease in anxiety to a decrease in the avoidance of predatory cat urine. The specific neurons that are infected with cysts, changes in circuits as a result of brain inflammation, and changes in the levels of systemic hormones are only a few of the reasons put forth to explain this change in mouse behavior. The observation of behavioral changes in mice infected with a non-persistent strain of T. gondii indicates that the location of the cysts is not what causes the behavioral changes, albeit no clear mechanism has yet been identified [2]. T. gondii has become a leading candidate due to several factors, including: (i) numerous studies have shown that people with schizophrenia have a higher prevalence of T. gondii than controls; (ii) some toxoplasmosis-infected individuals exhibit schizophrenia-like psychotic symptoms; (iii) there are many epidemiological similarities between toxoplasmosis and schizophrenia; and (iv) antipsychotic medications known to be effective (v) T. gondii infection has been shown to cause elevated dopamine levels in animal studies (dopamine spike is frequently seen in people with schizophrenia), and (vi) studies have revealed that people with schizophrenia have been exposed to cats more frequently than controls [10]. Although numerous studies have found that T. gondii-infected animals exhibit altered behavior, there is far less evidence that T. gondii affects human behavior. According to some researchers, having a positive serological test for T. gondii, or the presence of T. gondii antigens in the blood indicating a history of toxoplasmosis, is more commonly found in neuropsychiatric diseases, such as schizophrenia, Alzheimer's disease, and Parkinson's. However, some researchers have not discovered a connection between positive serological tests for T. gondii and cognition. Furthermore, the prevalence of numerous diseases believed to be associated with T. gondii seropositivity shows no difference between nations with high and low seropositivity levels [2]. A quarter of the studies also looked at a possible link between acute toxoplasmosis (IgM seropositivity) and schizophrenia. In comparison to controls, 5% on average of schizophrenia patients had toxoplasma IgM seropositivity. Fewer than 5% of the studies found a significant link between toxoplasma IgM seropositivity and schizophrenia [11].

Toxoplasmosis' potential biological contribution to schizophrenia has been the subject of speculation. Numerous experimental studies addressing the anatomical, histological, and physiological changes brought on by parasites have been published; however, the reported findings vary widely [12,13]. A recent meta-analysis revealed a correlation between the presence of schizophrenia and T. gondii infection with greater IgG levels [14]. The results of another meta-analysis study indicated that toxoplasmosis is linked to several psychiatric disorders and that latent
toxoplasmosis may reactivate in schizophrenia [15]. Another meta-analysis study published in 2022, reported that several observational studies found a small to significant association between toxoplasmosis and schizophrenia. Additional association studies were not justified, although significant methodological biases were found. It is recommended to investigate this link in clinical trials of first-line toxoplasma prophylaxis in seropositive patients with schizophrenia [11].

Nowadays, as in many fields of medicine, bibliometric studies have started to be published at increasing rates in the field of psychiatry [16-21]. Some bibliometric research has been conducted to better understand the literature on schizophrenia [21-23] or other neuropsychiatric disorders [24], however, there has been no comparable study in scientific publications investigating the relationship between schizophrenia and T. gondii.

MATERIALS AND METHODS
Toxoplasma gondii-related studies in schizophrenia were the focus of this bibliometric analysis study. In this bibliometric study, the research topic of T. gondii-related publications in schizophrenia during the last 32 years has been laid out, with the nations, organizations, authors, journals, and documents contributing to the basic knowledge structure.

Search Techniques
The Web of Science Core Collection (WOSCC) database was used to find T. gondii-related studies in schizophrenia.

This database was searched for pertinent articles on T. gondii-related studies in schizophrenia and exported on May 31, 2022.

PRISMA guidelines were followed in the conduct of this study. Two researchers independently assessed the caliber of the studies.

The following search approach was chosen: (TS = (T. gondii OR Toxoplasma gondii OR Toxoplasmosis)) AND TS = (schizophren*)—literary forms include standard articles, with no restriction on publishing language. For additional analysis, pertinent articles were exported and saved as plain.txt files, complete with full records and referenced references.

The term TS means ‘topic’ in the WOS search engine and searches title, abstract, author keywords, and keywords plus.

Inclusion criteria: Since the study query consisted of research articles and review articles, it was narrowed down to WOSCC indexes that only index articles [the Social Sciences Citation Index (SSCI), Emerging Sources Citation Index (ESCI), Arts & Humanities Citation Index (A&HCI, and Science Citation Index Expanded (SCIE)].

Exclusion criteria: Document types other than research articles and review articles and documents published before 1991 were excluded. Also, the publications indexed in other than ESCI, SCIE, AHCI, and SSCI indexes were excluded.

Bibliometric and visual analysis
Descriptive statistics were used to examine the study's characteristics.

Co-authorship analyses of countries and keyword co-occurrence analyses were carried out using the VOSviewer software 1.6.16 [25]. The VOSviewer focuses on visualizing bibliometric networks [26]. It can arrange several closely related nodes into various clusters, with the same hue indicating higher node correlation [25]. In this study, the VOSviewer software was used to create 1) a co-authorship network that examined the networks of collaboration between the countries and 2) a co-occurrence network that showed relationships between authors' keywords.

Also, to visualize the change in keywords and publisher countries over the years we used the bibliometric website [27]. For using this bibliometric website we also downloaded the data in tab-delimited format complete with full records and referenced references.

RESULTS
The investigation we conducted examined a total of 554 publications. 447 of them articles and 107 of them review articles. This field received contributions from 2396 authors across 881 organizations and 64 nations/regions. The most common language in which these publications are published is English, with 98.195%.

The first article was published in 1991, and since 2007, the number of articles has grown significantly. Since 2010, 482 publications have been published, representing 87% of all publications. Peaking in 2016, the number of publications remained irregular after 2016 and started to decline after 2020. In 2023, fewer than 10 articles were published, but an important point is that only the first five months of 2023 were completed at the time of the study. The number of citations started
to increase especially after 2011 and peaked in 2021. However, similar to the number of publications, the number of citations decreased significantly in 2022 and 2023.

The first publication was from the United States in 1991. From 1992 to 2001 there were no publications, while in 2001 there were publications from the United States and Germany. Between 2001 and 2021, publications were published every year, with the largest number of publications from the United States. The first publications from the Czech Republic were published in 2003. The first publications from the United Kingdom, Turkey, China, and Mexico were published in 2006. China produced the majority of the year 2022's publications. The annual publications on T. gondii-related studies in schizophrenia are shown in Figure 1a, together with their frequency and trends of the most publishing countries.

Figure 1b shows the annual publications on T. gondii-related studies in schizophrenia, as well as the number of citations to these papers worldwide.

The leading countries were the United States (n=236), the United Kingdom (n=49), Iran (n=44), China (n=38), Turkey and Germany (n=34), France (n=33), the Czech Republic (n=29), Australia (n=16), and Mexico (n=15). Each country or territory's number of articles is depicted in Figure 1a. Although the United States had the most publications (n =236), there was no published work from the United States between 1992-2000 and in the year 2002.

The leading institutions were Johns Hopkins University (the United States) (n=141), The University System of Maryland (the United States) (n=52), Charles University, Prague (Czech Republic) (n=27), Inserm, the French National Institute of Health & Medical Research (French), Udice French Research Universities (French) (n=25).

There were 547 funding organizations for these publications. The United States Department of Health and Human Services (n=79), the National Institutes of Health (n=77), the Stanley Institute for Medical Research (n=74), the National Institute of Mental Health (n=38), the National Natural Science Foundation of China (n=14), and the United Kingdom Research and Innovation provided the largest proportions of scientific funding.

The important keywords in the clusters were schizophrenia, toxoplasma gondii, toxoplasmosis, bipolar disorder, infection, toxoplasma, psychosis, inflammation, epidemiology, dopamine, depression, seroprevalence, parasite, meta-analysis, cognition, suicide, and behavior. 2015 was the year with the most keywords. The distribution of the frequency of keywords and keywords over the years can be seen in Figure 2 and Figure 3a, Figure 3b.

In total, 245 journals contributed to this field. Among these journals, the top five productive journals were Schizophrenia Research, Schizophrenia Bulletin, PLOS One, Folia Parasitologica, Brain, Behavior, and Immunity, and Parasites & Vectors (Figure 4).

The total number of citations was 21,218 and citations per publication was 38.3.

'The Environment and Susceptibility to Schizophrenia' published in 2011 [28] was the most cited publication, this publication received 439 citations. 'Prenatal Poly(I: C) Exposure and Other Developmental Immune Activation Models in Rodent Systems' was the 2nd most frequently cited article [29]. This publication also received 394 citations.

The top 10 most cited articles on schizophrenia and T. gondii are summarized in Table 1 at the level of number of citations, publication year, journal, and first author.

Maps with vosViewer
In total, 1078 keywords contributed to this field. When the search was narrowed down to keywords with at least 5 occurrences in the Vosviewer program, 59 keywords met this criterion. The term 'Toxoplasma gondii' was used in 206 documents, making it the most prolific keyword with 338 total link strength (TLS). Table 2 summarizes the frequency of keywords and TLS rates.

In total, 881 organizations contributed to this field. When the search was narrowed down to at least five publications in the Vosviewer program, 46 organizations published at least five articles. Johns Hopkins University published 141 publications and received 6976 citations. The largest bubble indicates the organization producing the most publications and the thickness of the lines indicates TLS (Figure 5a).

In total, 64 countries have contributed to this field. When the search was narrowed down to countries that published at least 5 articles in the Vosviewer program, 29 countries met this criterion. The United States was the most productive country with 236 documents, 13001 citations, and 122 TLS. The United Kingdom
published 47 articles and received 3142 citations. The co-authorship map between countries is visualized in Figure 5b. In Figure 5b, the largest bubble indicates the country producing the most publications and the thickness of the lines indicates TLS.

DISCUSSION
Numerous studies on humans, especially in the last 20 years, have investigated the potential link between toxoplasmosis, and schizophrenia [11]. Although there are published meta-analysis studies on this subject [11,14,15], our study is the first study in the accessible literature that examines scientific outcomes. The number of publications, highly active contributors (countries, authors, and institutions), top-cited articles, international collaborations, keywords, keyword plus, and the target journals for publication of the articles on toxoplasmosis and schizophrenia were all evaluated through this analysis. Therefore, it may be interesting to estimate the global and regional productivity of ongoing research on this topic.

More than 90% of the articles were in English, demonstrating once again that English is the most widely used academic language globally. This finding was similar to data from previous bibliometric studies [21,30,31,32-38].

Every year, 1 in 10,000 individuals (12 to 60 years old) develops schizophrenia. Based on a tight and exact description of the diagnosis, standardized assessment methodologies, and large, representative populations, the incidence rates appear consistent across countries, cultures, and time, at least for the last 50 years [39]. In this bibliometric analysis study, the evolution of publications on T. gondii in schizophrenia over the previous 32 years was examined. Over the past few decades, especially since 2007, articles on T. gondii-related publications in schizophrenia have shown an increasing tendency. After reaching a peak in 2016, the number of publications continued to fluctuate until 2020, after which it started decreasing.

This field received contributions from 2396 authors across 881 organizations and 64 nations/regions. Most of the pertinent publications in this bibliometric analysis were written by corresponding authors from several nations, including the United States, the United Kingdom, Iran, China, Turkey, Germany, France, and, the Czech Republic. We found that the countries and institutions that publish the most publications were from the United States and that the funding organizations were also from the United States.

According to a recent review study on T. gondii genotypes in Asia, numerous articles have described the spread of different T. gondii genotypes in different Chinese regions, however, there are a few documents for other Asian nations [40]. As a consequence of our research, we also discovered that, except in Iran, India, and China, no published articles on the connection between toxoplasmosis and schizophrenia were produced in Asian nations. There were no publications from the Central Asian nations (Kazakhstan, Turkmenistan, Tajikistan, and Kyrgyz Republic).

It's useful to examine the characteristics of international peer-reviewed journals to comprehend current trends [21,30,31,32-38]. Considering that toxoplasmosis is a parasitic disease and schizophrenia is a psychiatric disorder, it can be expected that most of the articles will be published in journals dealing with psychiatry and parasitology. The findings of our study were in this direction. Unsurprisingly, Schizophrenia Research was the most active journal with the greatest number of articles in other academic fields related to schizophrenia. It was also the most productive journal in the field of schizophrenia and T. gondii research. We found that the other top productive journals were Schizophrenia Bulletin, PLOS One, Folia Parasitologica, Brain, Behavior, and Immunity, and Parasites & Vectors.

The academic impact of publications may be reflected in citation analysis [33-35]. In this study, we analyzed the most cited articles. 'The Environment and Susceptibility to Schizophrenia’ published in 2011 [28] was the most cited publication, this publication received 439 citations. The study highlights how “schizophrenia” is linked to various problems, including the environment. The pathophysiology of schizophrenia has been extensively studied using animal models, and further research is currently being done. 'Prenatal Poly (I:C) Exposure and Other Developmental Immune Activation Models in Rodent Systems' was the second-most-cited article [29]. This publication also received 394 citations.

The proximity and prevalence of the study topics in scientific fields may be revealed by the co-occurrence analysis of keywords [41,42]. The important keywords in the clusters were ‘schizophrenia, toxoplasma gondii, toxoplasmosis, bipolar disorder, infection, toxoplasma, psychosis, inflammation, epidemiology, dopamine, depression, seroprevalence, parasite, meta-analysis, cognition, suicide, and behavior’.
Our understanding of the epidemiology of schizophrenia has grown dramatically in recent decades, and there is evidence that several widely held beliefs about its epidemiology are not correct. Nonetheless, significant gaps exist in the literature, particularly in underdeveloped nations. More population-based research employing widely acknowledged and verified detection technologies will be required to fill these gaps. Information on the disease's epidemiology, particularly when acquired from varied groups with varying exposure to probable risk factors, can assist in throwing light on the disease's origin and provide insight into viable preventive actions [43]. In our study, it was found that epidemiology and seroprevalence were among the frequently used keywords in the majority of publications on schizophrenia and toxoplasmosis. In particular, our analysis shows that publications on disease seroprevalence have been accelerating since 2003.

LIMITATIONS
There are a few limitations to this study. The data were first only collected from WOSCC and only the field indexes we selected belonging to WOSCC were searched. Despite being considered the most trustworthy database for bibliometric studies, WOS may still be missing some articles. Second, the bulk of the articles were published in English, which might have influenced the choice of language for publication. Third, there may be some discrepancies in various components; for instance, one institution might use numerous names over time.

CONCLUSION
In conclusion, more and more emphasis is being paid to the study of T. gondii's impact on schizophrenia. The significant increase in yearly publications implies that this research area has acquired importance on a global scale, with the United States having the most articles. The main organizations and researchers working on T. gondii studies on schizophrenia have been identified by this study. For new researchers and policymakers, these findings offer a thorough view of the larger picture of this study field. There have only been a few studies on the association between T. gondii and schizophrenia, thus further research is required to shed light on the pathophysiology of schizophrenia and the involvement of T. gondii in it. Researchers might learn more about this topic from the bibliometric analysis of the literature on toxoplasmosis and schizophrenia. It will also reveal the author and co-authorship network and help researchers worldwide find each other for potential research partnerships and grant-seeking collaboration.

FUNDING
None

AUTHOR CONTRIBUTIONS
SA and AEŞ wrote the manuscript and take full responsibility for the integrity of all parts of the manuscript.

CONFLICTS OF INTEREST
None

References


Figure 1a. Publication numbers of the frequently publishing countries.

Figure 1 b. The global number of publications and citations by years.
Figure 2. Frequently used keywords.

Figure 4. Frequently publishing journals.

Figure 5b. Co-authorship across countries.
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<td>Brown and Alan</td>
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<td>Prenatal maternal infection, neurodevelopment, and adult schizophrenia: a systematic review of population-based studies</td>
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1991-2023 ЖК. ТОКСОПЛАЗМОЗ ЖӘНЕ ШИЗОФРЕНИЯ БОЙЫНША ЖАРИЯLANЫМ БЕЛСЕНДІЛІГІ: БИБЛИОМЕТРИЯЛЫҚ ТАЛДАУ

Түйіндеме

Резюме
Шизофрения – сложное психическое состояние, характеризующееся признаками психоза, часто приводящее к социальному и профессиональному упадку. Шизофрения имеет сложную этиологию, которая является результатом взаимодействия факторов окружающей среды (например, инфекционных заболеваний) и генетической предрасположенности человека. Недавние эпидемиологические исследования показывают, что Toxoplasma gondii может вызывать шизофрению. Исследования, связанные с T. gondii при шизофрении, были в центре внимания этого исследования библиометрического анализа. Электронная база данных Web of Science использовалась для поиска исследований, связанных с T. gondii, при шизофрении. Анализ соавторства стран и анализ совпадения ключевых слов проводился с использованием программного обеспечения VOSviewer. В этом библиометрическом исследовании была изложена тема исследования публикаций о шизофрении, связанных с T. gondii, за последние 33 года, с указанием стран, организаций, авторов, журналов, основных ключевых слов, цитат и основных документов, вносящих вклад в основную информацию. Структура знаний. Значительное увеличение количества ежегодных публикаций означает, что эта область исследований приобрела важность в глобальном масштабе, при этом в Соединенных Штатах опубликовано больше всего статей. В ходе этого исследования были определены основные организации и исследователи, работающие над изучением шизофрении T. gondii. Результаты дают подробный обзор местности в этой области исследования.

Ключевые слова: Библиометрический анализ, шизофрения, токсоплазмоз, Toxoplasma gondii.

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