# RESEARCH

# Bibliometric and visual analysis of circadian rhythms in depression from 2004 to 2024

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# Abstract

Introduction Understanding the intricate relationship between circadian rhythms and depression is crucial for developing effective interventions and treatments for individuals affected by depression. Circadian rhythms regulate various physiological and behavioral processes, while depression manifests as persistent feelings of sadness and disturbances in sleep, appetite, and energy levels. Emerging research suggests a significant interplay between circadian rhythm disruption and depression, highlighting the need for comprehensive analysis in this area.

Methodology A bibliometric and visual analysis of literature on circadian rhythms in depression from 2004 to 2024 was conducted using the Web of Science Core Collection. Data were analyzed using bibliometric tools including VOSviewer, CiteSpace, and Bibliometrix to identify publication trends, geographical distribution, authorship patterns, institutional collaborations, journal preferences, keyword co-occurrence, and highly cited references.

**Results** Analysis revealed a steady increase in publications and citations related to circadian rhythms in depression. The United States emerged as the leading contributor, with strong global collaborations. Key journals included Chronobiology International and Journal of Affective Disorders. Top keywords included circadian rhythm, depression, sleep, melatonin, and bipolar disorder. The most cited article is a review titled "Practice parameters for the indications for polysomnography and related procedures: An update for 2005".

**Conclusions** This study offers a comprehensive overview of research on circadian rhythms in depression, highlighting key trends, contributors, and interdisciplinary intersections.

Keywords Depression, Circadian rhythms, Bibliometric, Visualize

# Introduction

Circadian rhythms, the innate biological oscillations that regulate physiological and behavioral processes over approximately a 24-hour cycle, play a pivotal role in orchestrating various bodily functions, including sleepwake patterns, hormone secretion, metabolism, and cognitive performance [1]. These rhythms are synchronized

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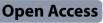
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with environmental cues, primarily light-dark cycles, through the master circadian pacemaker located in the suprachiasmatic nucleus (SCN) of the hypothalamus [2]. Disruptions in circadian rhythms, known as circadian misalignment or desynchronization, have been implicated in a myriad of health conditions, ranging from metabolic disorders to psychiatric illnesses [3, 4]. Among these psychiatric disorders, depression stands out as one of the most prevalent and debilitating mental health conditions worldwide [5]. Characterized by persistent feelings of sadness, despair, and loss of interest or pleasure in activities, depression exacts a substantial toll on individuals' functioning, relationships, and overall quality of



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life [6]. Despite advances in pharmacotherapy and psychotherapy, a significant proportion of individuals with depression fail to achieve remission or experience recurrence of symptoms, underscoring the need for innovative approaches to prevention and treatment [7].

Converging evidence from clinical and preclinical studies suggests that disruptions in circadian rhythms, known as circadian misalignment, may contribute to the pathogenesis of depression [3, 4, 8]. The seminal work of Terman [9] on light therapy for seasonal affective disorder (SAD) has been instrumental in establishing the efficacy of light therapy and its clinical applications. This review provides a comprehensive analysis of the evidence base for light therapy's antidepressant effects, highlighting the importance of light exposure timing and intensity. One retrospective analysis [10] demonstrated that seasonal variations significantly impact circadian rhythms and their association with depression severity, emphasizing the need to account for seasonal changes in longitudinal studies. Individuals with depression frequently exhibit disturbances in sleep architecture, such as insomnia or hypersomnia, as well as alterations in the timing of melatonin secretion and cortisol rhythms [8]. These abnormalities in circadian function are thought to interact with genetic predispositions, environmental stressors, and neurobiological pathways implicated in depression, exacerbating symptom severity and persisting the disorder [4, 11, 12]. One previous groundbreaking research by Fernandez et al. [13] has elucidated the distinct retina-brain pathways through which light affects mood and learning. This study reveals that different subpopulations of intrinsically photosensitive retinal ganglion cells (ipRGCs) drive the effects of light on learning and mood, with SCN-projecting ipRGCs affecting learning independently of the SCN's pacemaker function, and the ipRGC-PHb pathway driving light-mediated mood alterations. Conversely, the relationship between depression and circadian rhythms appears bidirectional, with depressive symptomatology also influencing circadian processes. Mood disturbances, such as persistent sadness or anhedonia, can disrupt the regularity of sleep-wake cycles and compromise the entrainment of circadian rhythms to environmental cues [11]. Moreover, alterations in circadian gene expression and SCN activity have been observed in animal models of depression, suggesting a reciprocal relationship between mood disorders and circadian dysfunction [1, 2, 12]. The intersection of circadian rhythms and depression holds significant implications for the development of novel therapeutic interventions and personalized treatment strategies [14]. Chronotherapeutic approaches, including bright light therapy, sleep deprivation, and timed administration of pharmacological agents, have demonstrated efficacy in modulating circadian rhythms and ameliorating depressive symptoms [14, 15]. By targeting circadian pathways implicated in mood regulation, these interventions offer promising avenues for enhancing treatment outcomes and addressing the heterogeneity of depression [16].

Understanding the complex interplay between circadian rhythms and depression holds immense promise for advancing our understanding of the etiology, course, and treatment of depression. By elucidating the mechanistic underpinnings linking circadian dysregulation to depressive symptomatology, researchers may uncover novel targets for pharmacological interventions or behavioral therapies aimed at restoring circadian homeostasis and relieving depressive symptoms. In recent years, the scientific community has witnessed a surge in research investigating circadian rhythms in depression, as evidenced by the proliferation of scholarly publications in this domain. Bibliometric and visual analysis methodologies offer powerful tools for systematically mapping the landscape of scientific inquiry, identifying key contributors, seminal works, and emerging trends, and delineating the intellectual structure of a research field [17, 18]. In this study, we embark on a comprehensive bibliometric and visual analysis of the literature on circadian rhythms in depression from 2004 to 2024. Leveraging cutting-edge bibliometric software such as CiteSpace, VOSviewer, and Bibliometrix, we aim to synthesize and analyze a vast corpus of scholarly publications retrieved from the Web of Science Core Collection. By employing citation analysis, coauthorship networks, keyword co-occurrence analysis, and other bibliometric techniques, we seek to unravel the patterns, trends, and dynamics shaping research on circadian rhythms in depression over the past two decades.

## Methods

### Data source and search strategy

In this study, all literature data were obtained from the Web of Science Core Collection (WOSCC), which serves as a critical global data source for literature retrieval [19, 20]. This database covers academic publications from over 200 different disciplinary fields worldwide. The literature bibliometric analysis in this study spans from January 1, 2004, to April 24, 2024. The search query used is as follows: TS = ("Circadian Rhythm" OR "Diurnal Rhythm" OR "Twenty Four Hour Rhythm" OR "Circadian Clocks" OR "Clock System") AND TS = ("depression" OR "depressive" OR "antidepressant"). Only English language literature was included in the search results, while documents categorized as letters, comments, or meetings were excluded.

### Data analysis

We exported and stored all literature information, including titles, authors, keywords, affiliations, countries/ regions, citations, journals, and publication dates, using Excel and plain text files. Subsequently, we analyzed and visualized the data using Microsoft Office Excel 2021, VOSviewer (version 1.6.18), CiteSpace (version 6.1.R6), and the R package "Bibliometrix".

CiteSpace, developed by Chaomei Chen, is used to create network maps of specific research fields to extract key information such as potential trends, frontiers, and research directions. In this study, the software was utilized for co-occurrence and clustering analysis of authorship, research institutions, and countries [21, 22]. VOSviewer, developed by Nees Jan van Eck and others in 2010, is a commonly used graphical tool for extracting and analyzing key information from numerous publications, including co-authorship networks, institutional collaborations, and co-occurrence of keywords [17, 23, 24]. "Bibliometrix", developed by Aria and Cuccurullo in 2017, was employed in this study to analyze the evolving trends of keywords in the literature. It is an R language tool used for comprehensive bibliometric and scientometric analysis [25].

### Results

# Publication and citation analysis

The trend in the number of publications and citations from 2004 to 2024 is depicted in Fig. 1 Overall, both the annual publication and citation counts show an increasing trend. The trend in publication counts exhibits some fluctuations, with each period spanning 5–6 years showing incremental growth. There are slight declines in 2011, 2016, and 2022, while in 2010, 2015, and 2021, the publication count increased significantly compared to the previous year, reaching peak values in those years as indicated by the peaks in the graph, with a peak of 136 articles/year reached in 2023. The citation frequency has increased year by year from 2004 to 2022, with significant increases observed in 2018–2019 and 2020–2021. The peak occurred in 2022 (7098 citations/year), with 2023 showing a similar level to 2021 (Fig. 1A).

Additionally, a polynomial fitting was performed on the cumulative annual publication count as shown in Fig. 1B, with the fitting formula:  $y = 2.6979 \times {}^{2} + 20.421x - 9.1684$ , and the goodness of fit ( $R^{2}$ ) was calculated to be 0.9994.

### Countries/regions analysis

To analyze the geographical origin of relevant publications, visualize the spatial distribution of research outcomes in the field, and understand global collaboration in this area, Supplementary Table 1 provides insight. In the field of circadian rhythms in depression research, the leading countries are the United States and the United Kingdom, both of which hold prominent positions in terms of publication volume and citation frequency internationally. For a more intuitive understanding, we conducted a detailed analysis of the top 30 countries by publication volume, as shown in Supplementary Fig. 1.

### **Author analysis**

The top ten authors ranked by publication volume and co-citation frequency were presented in Supplementary Table 2. The most prolific authors contributing to publications in this field include Eus J. W. Van Someren from the Netherlands Institute for Neuroscience, P. A. Geoffroy from Hôpital Bichat Claude-Bernard in France, Nakao Iwata from Fujita Health University in Japan, and Tsuyoshi Kitajima. All four authors have published 12 or more relevant articles in this field. Among the authors ranked high in co-citation frequency, Aj Lewy from Oregon Health and Science University in the United States (with 280 citations) and F. Benedetti from the University of Trieste in Italy (with 273 citations) receive significant attention. We also employed VOSviewer to visualize the collaboration network among these authors, as depicted in Supplementary Fig. 2.

### Institution analysis

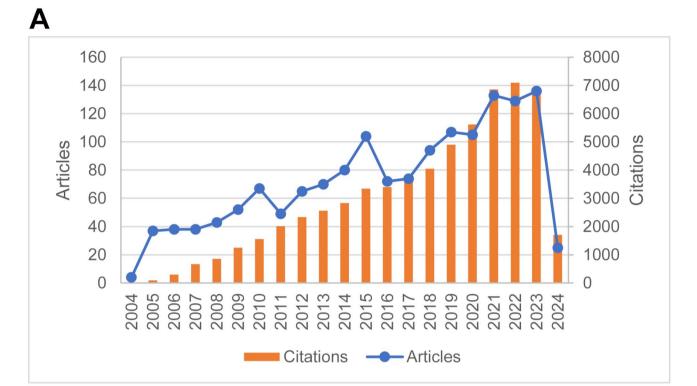
In Supplementary Table 3, we reported the top ten institutions ranked by the number of publications and total citations. It is evident from this table that institutions based in the United States dominate both in terms of publication volume and citation frequency. The top two institutions in terms of publication volume are the University of California, San Diego (38 papers) and the University of Pittsburgh (36 papers), both located in the United States, followed by the University of Toronto (30 papers) in Canada. In terms of total citations, the top four institutions are all based in the United States: The University of California, Los Angeles (3290 citations), Stanford University (2971 citations), the University of California, San Diego (2360 citations), and the University of Pittsburgh (2291 citations).

Visual analysis of the collaboration network among these institutions in Supplementary Fig. 3A reveals several clusters. Supplementary Fig. 3B further incorporates the temporal dimension into the spatial analysis presented in Supplementary Fig. 3A by highlighting the sequence of collaboration through colors.

### Journal analysis

Supplementary Table 4 presents the top ten journals in terms of publication and citation frequency in the field of circadian rhythms in depression. The journal with the highest output is *Chronobiology International* (77 articles), followed by *Journal of Affective Disorders* (50 articles) and *Psychoneuroendocrinology* (39 articles).

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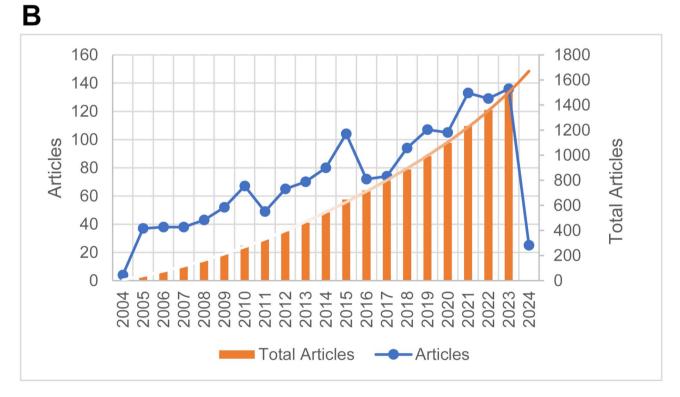


Fig. 1 Trends in the published articles and citation counts of circadian rhythms in depression from 2004 to 2024

(A) The annual publication quantity and citation frequency of circadian rhythms in depression from 2004 to 2024

(B) The annual publication quantity, cumulative publication quantity, and their polynomial fitting curves for researches of circadian rhythms in depression from 2004 to 2024

Supplementary Fig. 4A visualizes the relationships among journals that have published literature related to circadian rhythms in depression. Besides, Supplementary Fig. 4B categorizes journals related to researches of circadian rhythms in depression into three groups based on co-citation frequency. In the double-overlay of Supplementary Fig. 4C, citing journals are connected to cited journals through lines of varying thickness.

### **Keywords analysis**

Circadian rhythm appears most frequently (634 occurrences), nearly twice as much as the second-ranked keyword. Following closely are depression (339 occurrences), sleep (185 occurrences), melatonin (144 occurrences), and bipolar disorder (131 occurrences), all appearing over 100 times, indicating significant research hotspots in this field. The top 10 keywords in terms of occurrence frequency and total link strength were presented in Supplementary Table 5.

Figure 2 illustrates the co-occurrence relationships and strengths among keywords, with closely related keywords grouped into clusters. In Fig. 2A, the keyword circadian rhythm is at the center, with clinical researchrelated nouns such as behavior, serotonin, clock genes, and mouse forming the red cluster. The light blue cluster in the upper left mainly consists of nouns related to diseases and pathogenesis, such as melatonin, ramelteon, inflammation, Parkinson's disease, and Alzheimer's disease. The green cluster is associated with daily life and sleep issues: sleep, mood, insomnia, activity, and quality of life. Additionally, keywords related to adolescent life rhythms, such as bipolar disorder, chronobiology, chronotype, adolescence, children, and ADHD, form the blue cluster on the right. Keywords primarily associated with treating psychological problems or rhythm disorders, such as bright light therapy, chronotherapy, and mental health, form the purple cluster, while those related to mental stress form the yellow cluster: cortisol, stress, diurnal rhythm, and schizophrenia. Figure 2B and C provide insights into the contribution strengths of different keywords over time. Popular keywords in recent years include adolescence, mental health, chronotype, inflammation, sleep quality, aging, and pain.

Additionally, we list the top 25 keywords with the strongest burst citations in Fig. 2D. The burst periods of the top-ranked keywords, such as diurnal rhythm (burst strength 8.07), secretion (burst strength 7.84), and seasonal affective disorder (burst strength 9.97), all fall between 2004 and 2013. It's worth noting the keywords below the graph: validity (burst strength 5.31), physical activity (burst strength 6.63), anxiety (burst strength 5.43), sleep quality (burst strength 7.82), and mental health (burst strength 9.3), which remain at the forefront of research to this day.

### Highly cited references analysis

Table 1 lists the basic information of the top fifteen highly cited articles. The most cited article is a review titled "Practice parameters for the indications for polysomnography and related procedures: An update for 2005" by Kushida, CA et al. [26], published in Sleep in 2005 (1121 citations). In this article, the authors updated the practice parameters for polysomnography and related procedures, covering diagnostic categories related to sleep-disordered breathing, hypersomnia, parasomnias, periodic limb movement disorder, insomnia, depression, and circadian rhythm sleep disorders. This review laid the foundation for subsequent research in this field. The second most cited article is "The two-process model of sleep regulation: a reappraisal" [27] (755 citations), published in 2016 by Borbély, AA et al. in the Journal of Sleep Research. Despite being the most recent among the top fifteen highly cited articles, it demonstrates significant influence in the field. The authors proposed a reappraisal of the two-process model, highlighting its continued relevance in organizing thoughts on sleep regulation along two axes and its role in integrating the disciplines of sleep and rhythm research. Additionally, they provided evidence from animal experiments suggesting the involvement of the suprachiasmatic nucleus in regulating circadian rhythms in humans, thereby offering a theoretical foundation and research direction for the field of researches of circadian rhythms in depression. The third article, "Sleep and depression" [28] (747 citations), is a review published in the Journal of Clinical Psychiatry in 2005 by Tsuno, N et al. The authors conducted a comprehensive review of literature published in English or French between 1964 and 2005 on the relationship between sleep disorders and depression. Their analysis indicated a significant association between changes in sleep and depression, suggesting the need for further development of comprehensive depression models and new treatment approaches.

In CiteSpace, we analyzed the temporal relationships between different studies. As shown in Fig. 3A, the publication time of highly cited articles and their potential relationships are illustrated. Articles marked with purple circles signify their potential impact in driving the development of the field or serving as key turning points in academic research. This helps researchers in the field better understand the trends in its development.

In Fig. 3B, we further explore the potential relationships between the main contents of these studies, dividing them into 16 clusters based on their relevance. The most extensive theme is #0 human, which owes its emergence to early themes such as #1 bipolar disorder, #2 actigraphy, #4 circadian disruption, and #6 chronotype. Subsequently, from #0 human, there are explorations into related themes such as #3 melatonin, #7 genetics, #11 structure-activity relationships, and #13 chronotypes.

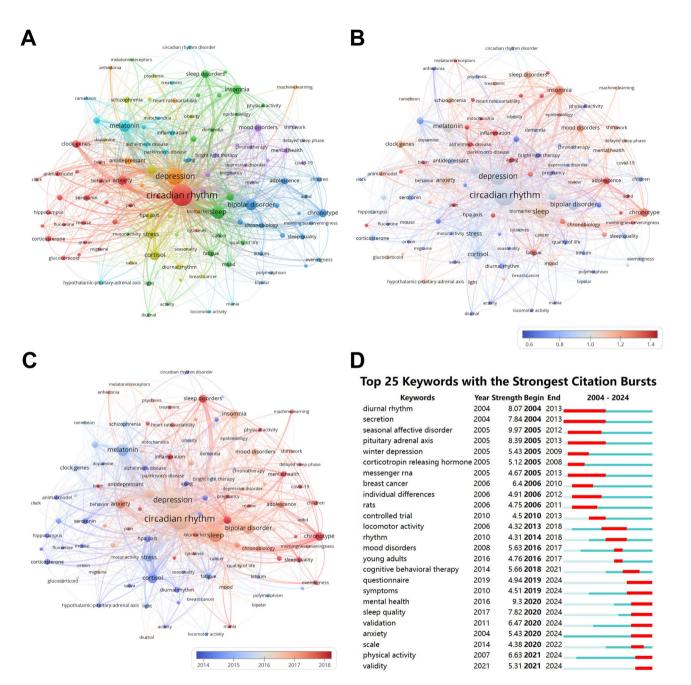


Fig. 2 Keywords co-occurrence network mapping of circadian rhythms in depression from 2004 to 2024

(A) The keyword map of circadian rhythms in depression visually displays the connections among studied keywords. Nodes, distinguished by various colors, represent different keyword clusters. Node size reflects co-occurrence frequency, and connections between nodes depict relationships among keywords

(B) The figure depicts keywords' recent contributions to researches of circadian rhythms in depression relative to their overall output from 2004 to 2024, with a red bias indicating increased influence and a blue bias suggesting decreased activity in the field. The color scale reflects the ratio of keywords over the past five years, highlighting institutions with notable impacts or reduced involvement in this study

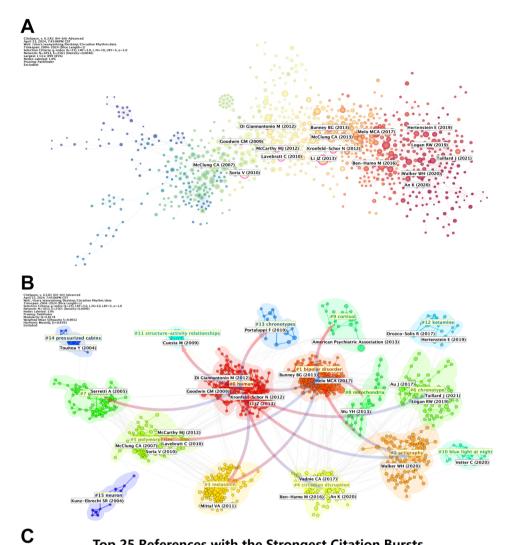
(C) Keywords heat map on researches of circadian rhythms in depression

(D) The diagram illustrates the 25 primary keywords characterized by pronounced bursts of citations, denoted by red spikes on the timeline. These spikes signify sudden surges in citation counts, signaling pivotal moments of emerging crucial questions or solutions within the field

In Fig. 3C, the burst situation of citations is illustrated. The earliest burst occurred in 2006 with Nievergelt, CM et al.'s article "Suggestive evidence for association of the circadian genes PERIOD3 and ARNTL with bipolar disorder" published in the American Journal of Medical Genetics Part B-Neuropsychiatric Genetics [29] (burst strength 8.44). The longest burst duration is associated with Soria, V et al.'s 2010 publication

Table 1	1 Ranking of the top fifteen major highly of	Ranking of the top fifteen major highly cited references of circadian rhythms in depression from 2004 to 2024	2004 to 2024	,			
Rank	Author		Source Title	Cited	Year	Category	DOI
<del>.</del>	Kushida, CA; Littner, MR; Morgenthaler, T; Alessi, CA; Bailey, D; Coleman, J; Friedman, L; Hirshkowitz, M; Kapen, S; Kramer, M; Lee- Chiong, T; Loube, DL; Owens, J; Pancer, JP; Wise, M	Practice parameters for the indications for polysomnography and related procedures: An update for 2005	Sleep	1121	2005	Review	https://doi.org/10.1 093/sleep/28.4.499
7	Borbély, AA; Daan, S; Wirz-Justice, A; Deboer, T	The two-process model of sleep regulation: a reappraisal	Journal of Sleep Research	755	2016	Article	https://doi.org/10.1 111/jsr.12371
ŝ	Tsuno, N; Besset, A; Ritchie, K	Sleep and depression	Journal of Clinical Psychiatry	747	2005	Review	https://doi.org/10.4 088/JCP:v66n1008
4	Wulff, K; Gatti, S; Wettstein, JG; Foster, RG	Sleep and circadian rhythm disruption in psychiatric and neurodegenerative disease PERSPECTIVES	Nature Reviews Neuroscience	697	2010	Article	https://doi.org/10.1 038/nrn2868
Ŋ	Pandi-Perumal, SR; Srinivasan, V; Maestroni, GJM; Cardinali, DP; Poeggeler, B; Hardeland, R	Melatonin - Nature's most versatile biological signal?	Febs Journal	671	2006	Review	https://doi.org/10.1 111/j.1742-4658.200 6.05322.x
Q	Clow, A; Thorn, L; Evans, P; Hucklebridge, F	The awakening cortisol response: Methodological issues and significance	Stress-The International Journal on The Biology of Stress	643	2004	Review	https://doi.org/10.1 080/1025389041000 1667205
~	Gallego, M; Virshup, DM	Post-translational modifications regulate the ticking of the circadian clock	Nature Reviews Molecular Cell Biology	624	2007	Review	https://doi.org/10.1 038/nrm2106
ω	Buckley, TM; Schatzberg, AF	Review: On the interactions of the hypothalamic-pituitary- adrenal (HPA) axis and sleep: Normal HPA axis activity and circadian rhythm, exemplary sleep disorders	The Journal of Clini- cal Endocrinology and Metabolism	609	2005	Review	https://doi.org/10.1 210/jc.2004 – 1056
6	Pandi-Perumal, SR; Trakht, I; Srinivasan, V; Spence, DW; Maestroni, GJM; Zisapel, N; Cardinali, DP	Physiological effects of melatonin: Role of melatonin recep- tors and signal transduction pathways	Progress in Neurobiology	576	2008	Review	https://doi.org/10.1 016/j.pneurobio.200 8.04.001
10	Riemersma-van Der Lek, RF; Swaab, DF; Twisk, J; Hol, EM; Hoogendijk, WJG; Van Someren, EJW	Effect of bright light and melatonin on cognitive and non- cognitive function in elderly residents of group care facilities - A randomized controlled trial	JAMA-Journal of the Ameri- can Medical Association	501	2008	Article	https://doi.org/10 .1001/jama.299.22 .2642
11	Drake, CL; Roehrs, T; Richardson, G; Walsh, JK; Roth, T	Shift work sleep disorder: Prevalence and consequences beyond that of symptomatic day workers	Sleep	501	2004	Article	https://doi.org/10.1 093/sleep/27.8.1453
12	Dubocovich, ML; Delagrange, P; Krause, DN; Sugden, D; Cardinali, DP; Olcese, J	International Union of Basic and Clinical Pharmacology. LXXV. Nomenclature, Classification, and Pharmacology of G Protein- Coupled Melatonin Receptors	Pharmacological Reviews	435	2010	Review	https://doi.org/10.1 124/pr.110.002832
13	Martin, JL; Hakim, AD	Wrist Actigraphy	Chest	414	2011	Article	https://doi.org/10.1 378/chest.10-1872
14	Germain, A; Kupfer, DJ	Circadian rhythm disturbances in depression	Human Psychophar- macology-Clinical and Experimental	408	2008	Review	https://doi.org/10.1 002/hup.964
15	Johnson, EO; Roth, T; Schultz, L; Breslau, N	Epidemiology of DSM-IV insomnia in adolescence: Lifetime prevalence, chronicity, and an emergent gender difference	Pediatrics	402	2006	Article	https://doi.org/10.1 542/peds.2004-2629

Table 1 Banking of the top fifteen major highly cited references of circadian rhythms in depression from 2004 to 2024



# Top 25 References with the Strongest Citation Bursts

References	Year	Strength Begin End	2004 - 2024
Nievergelt CM, 2006, AM J MED GENET B, V141B, P234, DOI 10.1002/ajmg.b.30252, DOI	2006	8.44 2007 201	1
McClung CA, 2007, PHARMACOL THERAPEUT, V114, P222, DOI 10.1016/j.pharmthera.2007.02.003, DOI 2	2007	15.86 2008 201	2
Roybal K, 2007, P NATL ACAD SCI USA, V104, P6406, DOI 10.1073/pnas.0609625104, DOI	2007	7.42 2008 201	2
Soria V, 2010, NEUROPSYCHOPHARMACOL, V35, P1279, DOI 10.1038/npp.2009.230, DOI	2010	10.38 2010 201	5
Germain A, 2008, HUM PSYCHOPHARM CLIN, V23, P571, DOI 10.1002/hup.964, DOI	2008	8.77 2010 201	3
Kasper S, 2010, J CLIN PSYCHIAT, V71, P109, DOI 10.4088/JCP.09m05347blu, DOI	2010	8.37 2010 201	4
Kripke Daniel F, 2009, J CIRCADIAN RHYTHMS, V7, P2, DOI 10.1186/1740-3391-7-2, DOI	2009	7.93 2010 201	4
Wulff K, 2010, NAT REV NEUROSCI, V11, P589, DOI 10.1038/nrn2868, DOI	2010	9.19 2012 201	5
de Bodinat C, 2010, NAT REV DRUG DISCOV, V9, P628, DOI 10.1038/nrd3140, DOI	2010	9.19 2012 201	5
Portaluppi F, 2010, CHRONOBIOL INT, V27, P1911, DOI 10.3109/07420528.2010.516381, DOI	2010	7.8 2012 201	5
Lavebratt C, 2010, PLOS ONE, V5, P0, DOI 10.1371/journal.pone.0009407, DOI	2010	7.8 2012 201	5
McCarthy MJ, 2012, J BIOL RHYTHM, V27, P339, DOI 10.1177/0748730412456367, DOI	2012	8.17 2013 201	7
Li JZ, 2013, P NATL ACAD SCI USA, V110, P9950, DOI 10.1073/pnas.1305814110, <u>DOI</u>	2013	16.46 2014 201	8
McClung CA, 2013, BIOL PSYCHIAT, V74, P242, DOI 10.1016/j.biopsych.2013.02.019, DOI	2013	12 2014 201	8
American Psychiatric Associati AL OF MENTAL DISORDERS, V5, P0, DOI	2013	10.39 2014 201	8
Ng TH, 2015, SLEEP MED REV, V20, P46, DOI 10.1016/j.smrv.2014.06.006, DOI	2015	8.17 2016 202	0
Melo MCA, 2017, SLEEP MED REV, V34, P46, DOI 10.1016/j.smrv.2016.06.007, DOI	2017	13.6 2018 202	2
Moon JH, 2016, EBIOMEDICINE, V11, P285, DOI 10.1016/j.ebiom.2016.08.019, DOI	2016	7.58 2018 202	1
Lyall LM, 2018, LANCET PSYCHIAT, V5, P507, DOI 10.1016/S2215-0366(18)30139-1, DOI	2018	10.73 2019 202	4
Takaesu Y, 2018, PSYCHIAT CLIN NEUROS, V72, P673, DOI 10.1111/pcn.12688, DOI	2018	7.82 2019 202	2
Vadnie CA, 2017, NEURAL PLAST, V2017, P0, DOI 10.1155/2017/1504507, DOI	2017	8.41 2020 202	2
Walker WH, 2020, TRANSL PSYCHIAT, V10, P0, DOI 10.1038/s41398-020-0694-0, DOI	2020	15.98 2021 202	4
Difrancesco S, 2019, DEPRESS ANXIETY, V36, P975, DOI 10.1002/da.22949, DOI	2019	7.48 2021 202	4
Crouse JJ, 2021, LANCET PSYCHIAT, V8, P813, DOI 10.1016/S2215-0366(21)00034-1, DOI	2021	7.98 2022 202	4
Logan RW, 2019, NAT REV NEUROSCI, V20, P49, DOI 10.1038/s41583-018-0088-y, <u>DOI</u>	2019	7.98 <b>2022</b> 202	4

Fig. 3 (See legend on next page.)

(See figure on previous page.)

Fig. 3 Highly cited references co-citation network mapping of circadian rhythms in depression from 2004 to 2024

(A) Application of citespace, literature relation network diagram. The different colors of the nodes indicate additional years, from blue to red, the later. The node size indicates the frequency of the reference

(B) The keyword heatmap displays topics, with smaller numbers indicating larger clusters, and #0 representing the largest cluster. Node size reflects cocitation frequency, and the links between nodes signify co-citation relationships

(C) The diagram illustrates the 25 primary references characterized by pronounced bursts of citations, denoted by red spikes on the timeline. These spikes signify sudden surges in citation counts, signaling pivotal moments of emerging crucial questions or solutions within the field

in Neuropsychopharmacology titled "Differential Association of Circadian Genes with Mood Disorders: CRY1 and NPAS2 are Associated with Unipolar Major Depression and CLOCK and VIP with Bipolar Disorder" [30] (burst strength 10.38), and their 2018 publication in Lancet Psychiatry titled "Association of disrupted circadian rhythmicity with mood disorders, subjective wellbeing, and cognitive function: a cross-sectional study of 91105 participants from the UK Biobank" authored by Lyall, LM et al. [31] (burst strength 10.73). These two articles had bursts lasting for six years, and notably, the latter still receives significant attention to this day. Additionally, the four articles at the bottom of the graph are still in their burst periods.

### Discussion

Our comprehensive bibliometric and visual analysis of the literature on circadian rhythms in depression from 2004 to 2024 has provided valuable insights into the evolving landscape of research in this field. By synthesizing data from scholarly publications retrieved from the Web of Science Core Collection and leveraging advanced bibliometric techniques and visualization tools, including CiteSpace, VOSviewer, and Bibliometrix, we have elucidated key trends, thematic clusters, and interdisciplinary intersections shaping research on the intersection of circadian rhythms and depression.

One notable finding of our study is the upward trajectory in both the number of publications and citations related to circadian rhythms in depression over the past two decades. This trend underscores the growing recognition of the importance of circadian processes in understanding the pathophysiology and treatment of depression. The significant increase in publication counts in recent years, particularly from 2010 onwards, reflects heightened research activity and interest in this area. This surge may be attributed to several factors, including advancements in chronobiology research methodologies, increased awareness of the role of circadian dysregulation in mental health, and the translation of preclinical findings into clinical applications [11]. Moreover, the exponential growth in citation frequency, especially in the latter half of the analyzed period, indicates the increasing impact and influence of research on circadian rhythms in depression within the scientific community. The peak in citation frequency observed in 2022 suggests that seminal studies and review articles published around this time have garnered substantial attention and recognition, shaping subsequent research directions and hypotheses. For instance, the review by McClung (2007) on circadian genes and the biology of mood disorders has been cited extensively, highlighting its pivotal role in synthesizing existing knowledge and stimulating further investigations [3].

Our analysis revealed the dominance of certain countries, institutions, and authors in the literature on circadian rhythms in depression. Notably, the United States emerged as the leading contributor, both in terms of publication volume and citation frequency. This finding underscores the significant investment and expertise in circadian research within the U.S. academic and clinical communities. Institutions such as the University of California, San Diego, and Stanford University have consistently produced high-impact research in this field, as evidenced by their large publication output and citation counts. Several prolific authors have also made substantial contributions to the literature on circadian rhythms in depression. Eus J. W. Van Someren, P. A. Geoffroy, and Aj Lewy are among the most prominent figures in this domain, with multiple publications and high co-citation frequencies. Their work spans various aspects of circadian biology, from basic mechanisms to clinical applications, and has significantly advanced our understanding of the complex relationship between circadian rhythms and mood disorders.

Our analysis of collaboration networks among countries, institutions, and authors revealed vibrant interdisciplinary interactions within the field of circadian rhythms in depression research. Clusters of collaborative relationships, characterized by strong ties between researchers and institutions, highlight the importance of teamwork and knowledge exchange in advancing scientific discoveries. For example, the blue and purple clusters representing institutions such as the University of California, San Diego, and the University of Michigan highlight close collaborations among leading research centers in the United States and abroad. Interdisciplinary intersections were also evident in the thematic clusters identified in our analysis. The co-occurrence of keywords related to neuroscience, psychiatry, endocrinology, and genetics reflects the multifaceted nature of circadian rhythms in depression research [32]. Moreover, the emergence of novel themes such as chronotherapy, genetics of mood disorders, and circadian disruption underscores the

ongoing exploration of innovative research paradigms and treatment modalities [14].

Recent advancements in the field of circadian rhythms and depression have highlighted the pivotal role of wearable technology and AI in understanding and managing these disorders. Actigraphy, a form of wearable technology, has long been a crucial tool for assessing sleep and activity patterns, providing objective measures of rest-activity cycles that are essential for elucidating the relationship between circadian misalignment and depressive symptoms [33]. Building on this foundation, the integration of AI with data from commercial wearable devices has ushered in new opportunities for large-scale data analysis and the identification of subtle patterns in behavior and activity. This technological leap enables the examination of larger, more diverse datasets, potentially revealing nuanced aspects of circadian rhythms and their impact on depression [34]. For instance, longitudinal assessments using multimodal wearable sensing have shown that seasonal variations significantly impact circadian rhythms and their associations with depression severity, emphasizing the need to account for seasonal changes in longitudinal studies [10]. Additionally, studies have explored the causal dynamics of sleep, circadian rhythm, and mood symptoms in patients with major depression and bipolar disorder, finding that circadian phase disturbances directly precede mood symptoms in patients with major depressive disorder (MDD) and bipolar disorder type I (BDI), but not in patients with bipolar disorder type II (BDII) [35]. This suggests that targeting circadian rhythms could be a potential therapeutic strategy for managing mood disorders effectively. Another study showed that a lower circadian quotient, reflecting less robust rhythmicity, was associated with improvement in depression after the first week of treatment [36]. Although this study did not find a significant association with long-term treatment outcomes, it highlights the potential of using wearable devices to monitor real-time changes in depression severity, which could be particularly beneficial for timely mental health care. Finally, models developed using sleep-wake data from wearable devices have achieved high accuracy in predicting depressive, manic, and hypomanic episodes, with circadian phase shifts being the most significant predictors [37]. These findings collectively underscore the potential of wearable devices and AI in advancing our understanding of circadian rhythms and their impact on depression.

Our findings are further supported by recent studies utilizing data from the UK Biobank (UKB), which have explored the intricate relationship between circadian rhythms, sleep patterns, and mental health outcomes. Disrupted circadian rhythmicity is reliably associated with various adverse mental health outcomes, including major depressive disorder and bipolar disorder, underscoring the importance of circadian rhythms in mental health and highlighting the potential for circadian-based interventions to improve mood and wellbeing [31]. Greater daytime light exposure is associated with better mood, sleep quality, and earlier chronotype, suggesting that optimizing light exposure during the day could be a simple yet effective strategy for improving mental health and reducing the risk of mood disorders [38]. Additionally, machine learning approaches have identified the most predictive sleep and circadian parameters for depression-related outcomes, highlighting several clinically relevant features associated with depression and its severity [39]. Sleep pattern differences have also been found to be a transdiagnostic feature of individuals with lifetime mental illness, emphasizing the critical role of circadian rhythms and sleep patterns in mental health [40]. Collectively, these studies provide a foundation for future research aimed at developing circadian-based interventions and predictive models for mood disorders. The findings of our study have several implications for future research directions and clinical practice in the field of circadian rhythms and depression. First, the identification of research trends and hotspots can guide researchers and funding agencies in prioritizing areas with the greatest potential for impact. For example, the increasing focus on chronotherapeutic interventions and genetic determinants of circadian dysfunction underscores the need for translational research that bridges basic science with clinical applications [14]. Second, the establishment of collaborative networks and interdisciplinary partnerships can facilitate knowledge exchange and accelerate the pace of discovery. By fostering collaborations between researchers from diverse backgrounds, institutions, and countries, stakeholders can leverage complementary expertise and resources to tackle complex research questions and address unmet clinical needs [41]. Third, the integration of circadian biology into clinical practice holds promise for optimizing the management of depression and related mood disorders [3]. Chronotherapeutic interventions, such as light therapy, sleep manipulation, and pharmacological agents targeting circadian pathways, offer novel avenues for personalized treatment approaches [14]. Moreover, the identification of circadian biomarkers and genetic markers of treatment response may enable more precise diagnostics and tailored interventions for individuals with depression [15, 32].

several limitations should be acknowledged. First, our study focused exclusively on publications indexed in the Web of Science Core Collection, potentially overlooking relevant literature published in other databases or non-indexed journals. Future studies may benefit from incorporating a broader range of data sources to provide a more comprehensive overview of research in this field. Second, the reliance on bibliometric data and quantitative analyses may overlook qualitative aspects of research, such as the clinical significance of findings or the impact on patient outcomes. Integrating qualitative assessments and expert opinions into future analyses can provide a more nuanced understanding of the implications of circadian rhythms in depression research. Finally, the dynamic nature of scientific research necessitates ongoing updates and re-evaluations of research trends and patterns over time. Longitudinal studies tracking changes in publication trends, citation networks, and thematic clusters can elucidate evolving research priorities and emerging areas of interest in circadian rhythms and depression.

### Conclusion

our study offers a comprehensive overview of research on circadian rhythms in depression, highlighting key trends, contributors, and interdisciplinary intersections. By elucidating the complex relationship between circadian biology and mood disorders, our findings pave the way for future investigations aimed at unraveling the underlying mechanisms of depression and developing innovative therapeutic interventions.

### Supplementary Information

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Supplementary Material 1

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None.

### Author contributions

Cong Zhou: Conceptualization, Funding acquisition, Investigation, Validation, Formal analysis, Writing-original draft. Shanling Ji: Resources, Methodology, Software, Data curation, Formal analysis. Aoxue Zhang: Data curation, Resources. Hao Yu: Resources, Writing-review and editing. Chuanxin Liu: Supervision, validation. Sen Li: Conceptualization, Investigation, Data curation, Writing-review and editing, Methodology, Project administration.

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### Data availability

Data are available upon reasonable request from the corresponding author.

### Declarations

**Ethics approval and consent to participate** Not applicable.

### **Consent for publication**

Not applicable.

#### **Competing interests**

The authors declare no competing interests.

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