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Circadian Disruption and the Gut–Liver Axis: Linking Modern Lifestyle, Microbiome Dysbiosis, and Metabolic Liver Health

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A B S T R A C T

Circadian disruption caused by modern lifestyle factors, including shift work, irregular sleep patterns, and altered meal timing, has been increasingly associated with metabolic disturbances. This narrative review aims to summarize the current evidence regarding the relationship between circadian disruption, gut microbiome alterations, and metabolic liver health through the gut-liver axis. Literature searches were conducted using PubMed, Scopus, and Google Scholar databases with relevant keywords related to circadian rhythm, gut microbiome, chrononutrition, and liver metabolism. A total of 18 articles published between 2020 and 2025 were included and analyzed descriptively. Current evidence indicates that circadian disruption is associated with changes in gut microbial composition, inflammatory regulation, bile acid metabolism, and hepatic metabolic homeostasis.

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INTRODUCTION

Circadian organization is essential for maintaining the temporal coordination of physiological processes, including sleep–wake regulation, feeding behavior, endocrine activity, immune function, and metabolic homeostasis. The circadian system enables organisms to anticipate daily environmental changes through coordinated interactions between the central clock located in the suprachiasmatic nucleus and peripheral clocks present in metabolic organs. However, modern lifestyles have increasingly introduced conditions that disturb circadian alignment, including rotating shift work, irregular sleep schedules, artificial light exposure at night, and inconsistent meal timings. These disturbances may create a mismatch between endogenous biological rhythms and externally imposed behavioral schedules, potentially affecting metabolism. Sinturel et al. (2022) described circadian rhythms as essential regulators of metabolic pathways, including glucose metabolism, lipid homeostasis, and energy utilization. Their review emphasized that disruption of circadian coordination may contribute to metabolic dysfunction through impaired temporal regulation of physiological processes, highlighting the circadian rhythm as an important component of metabolic health.

Circadian disruption may influence metabolic health beyond sleep-related consequences because peripheral organs, particularly the liver and gastrointestinal tract, possess intrinsic and rhythmic regulation. The liver exhibits circadian control over the metabolic processes involved in glucose production, lipid synthesis, cholesterol metabolism, and detoxification pathways. Gastrointestinal function is influenced by feeding schedules, intestinal motility, microbial activity, and host-derived circadian signals. Zhao et al. (2022) reviewed the role of circadian rhythms in metabolic diseases and emphasized that the disruption of peripheral clocks through irregular sleep and feeding patterns may alter metabolic flexibility and contribute to disease susceptibility. Their findings suggest that nutritional timing, rather than nutritional composition alone, is an important regulator of metabolic adaptation. Therefore, disturbances in sleep and meal timing may influence communication between metabolic organs and contribute to systemic metabolic imbalances.

Recent evidence has increasingly demonstrated the interaction between circadian regulation and the gut microbiota. The intestinal microbial ecosystem exhibits rhythmic fluctuations that are influenced by feeding behavior, host circadian signals, and environmental factors. Vivarelli et al. (2025) investigated the effects of acute sleep–wake cycle disruption on the human gut microbiome and reported alterations in microbial functional profiles and interaction networks following circadian misalignment. Although major changes in the overall microbial composition were limited, this study demonstrated that short-term disruption of biological timing could influence microbial function and community organization. These findings are important because they suggest that circadian disturbance may affect intestinal microbial activity before the development of measurable clinical changes. However, existing human studies are limited, particularly regarding the long-term impact of persistent lifestyle-related circadian disruption on gut microbial regulation.

The gut-liver axis provides an important framework for understanding how intestinal microorganisms may influence hepatic metabolism through microbial-derived metabolites, bile acid signaling, immune regulation, intestinal barrier function, and portal circulation. Hsu & Schnabl (2023) reviewed the role of the gut microbiota in liver health and disease, emphasizing that microbial imbalance may contribute to hepatic inflammation and metabolic disturbances through altered microbial products and immune signaling. Furthermore, Gu & Wu (2025) described the gut-liver axis as a complex physiological network involving anatomical, immunological, and metabolic interactions between the intestine and liver. These studies highlight that intestinal microbial alterations are not isolated gastrointestinal events but may influence systemic metabolic regulation, including hepatic function. Nevertheless, current evidence regarding circadian disruption, gut microbiome alterations, and liver metabolism remains fragmented because most studies have investigated these components separately rather than as an interconnected biological pathway.

Despite growing interest in circadian biology, microbiome research, and metabolic liver disorders, several knowledge gaps remain. Previous studies have provided important insights into the circadian regulation of metabolism, microbial responses to sleep disruption, and gut-liver communication; however, an integrated understanding of how modern lifestyle-related circadian disruption influences the gut-liver axis is still limited. Most available evidence focuses either on specific exposures, such as shift work or sleep restriction, or on established metabolic diseases rather than early metabolic alterations associated with disrupted biological timing. Therefore, this narrative review aims to synthesize current evidence regarding the relationship between circadian disruption, gut microbiome alterations, and metabolic liver health through the gut-liver axis framework. This review discusses the potential mechanisms involving circadian misalignment, chrononutrition, microbial-derived metabolites, inflammatory regulation, and hepatic metabolic pathways to provide a comprehensive perspective on how modern lifestyle patterns may influence gastrointestinal and hepatic health.

LITERATUR REVIEW

Circadian rhythm disruptions caused by modern lifestyles—such as exposure to artificial light at night, irregular eating patterns (failure to follow time-restricted feeding), and shift work—are known to be closely linked to the gut-liver axis. These circadian disruptions trigger dysbiosis in the gut microbiome, which in turn impairs intestinal membrane permeability (leaky gut) and increases the translocation of endotoxins such as lipopolysaccharides (LPS) into the portal venous system. Constant exposure to these pathogenic metabolites and inflammatory mediators induces an immune response through the development of systemic inflammation and oxidative stress in liver tissue. Consequently, this disrupted axis accelerates lipid accumulation and exacerbates the progression of various metabolic liver dysfunctions, including Non-Alcoholic Fatty Liver Disease.

METHODOLOGY

This descriptive study was conducted using a narrative review method (Theile & Beall, 2024). The literature search was conducted from January to March 2026 to identify current evidence regarding the relationship between circadian disruption, gut microbiome alterations, and metabolic liver health through the gut-liver axis framework. Literature searches were performed using electronic databases, including PubMed, Scopus, and Google Scholar. The search strategy was developed using combinations of keywords related to circadian rhythm, gut microbiome, chrononutrition, and liver metabolism, including:

("*Circadian Disruption*" OR "*Circadian Rhythm*" OR "*circadian misalignment*") AND ("*Gut Microbiome*" OR "*Intestinal Microbiota*") AND ("*Gut-liver Axis*" OR "*Liver Metabolism*" OR "*Metabolic Liver Disease*")

The literature selection process was conducted based on predefined inclusion and exclusion criteria as follows. Articles were screened through title and abstract evaluation, followed by full-text assessment to determine their eligibility. Eighteen articles published between 2020 and 2025 were included and descriptively analyzed. The population in this review consisted of scientific articles discussing the relationship between circadian disruption, gut microbiome regulation, and hepatic metabolic health. The sample for this review consisted of selected articles that fulfilled the established eligibility criteria. The inclusion and exclusion criteria were as follows.

1. Inclusion Criteria
    a. Articles published in the English language.
    b. Articles published between 2020 and 2025 were included.
    c. Original research articles and review articles discussing circadian rhythm disruption, gut microbiome, chrononutrition, gut-liver axis, and metabolic liver health.
    d. Articles available in the full-text format.
    e. Human and relevant experimental studies have investigated the mechanisms related to circadian regulation, microbiome alteration, and hepatic metabolism.
2. Exclusion Criteria
    a. Articles without accessible full-text versions were excluded.
    b. Articles unrelated to the relationship between circadian disruption, the gut microbiome, and liver metabolism.
    c. Duplicate publications.
    d. Conference abstracts, editorials, letters, and non-scientific publications were excluded.
    e. Systematic reviews or meta-analyses that did not provide original data relevant to the mechanisms discussed.

RESEARCH RESULT AND DISCUSSION

Circadian Disruption and Gut Microbiome Alteration

Table 1. Characteristics of Literature Evaluating Circadian Disruption and Gut Microbiome Alteration

No	Author (Year)	Study Design	Model/Population	Main Findings
1	(Liu et al., 2020)	Human experimental study	22 healthy adults	Sleep–wake cycle shift alters gut microbiome functional profiles and microbial interaction networks. Changes were detected mainly in microbial function rather than large taxonomic composition changes.
2	(Aguilar-López et al., 2020)	Narrative review	Human and animal studies	Sleep and circadian rhythms influence the gut microbiota through feeding timing, immune regulation, and metabolic pathways.
3	(Murakami & Tognini, 2020)	Literature review	Human and experimental evidence	Circadian misalignment and gut microbiota influence each other bidirectionally and may contribute to inflammation and metabolic disorders.
4	(Pearson et al., 2020)	Narrative review	Human and animal evidence	Circadian rhythms regulate microbial oscillations, whereas microbiota-derived signals influence host metabolism and disease susceptibility.
5	(Withrow et al., 2021)	Narrative review	Human and non-human studies	Sleep deficiency and circadian disruption modify microbial diversity, metabolite composition, and

				metabolic regulation.
6	(Daas & De Roos, 2021)	Mechanistic review	Microbiome experimental studies	The gut microbiota mediates the relationship between dietary timing and host circadian metabolism.
7	(Choi et al., 2021)	Review article	Microbiome and metabolic studies	The circadian clock and gut microbiome coordinate metabolic responses to dietary signals.
8	(Litichevskiy & Thaiss, 2022)	Review article	Microbiome circadian studies	The gut microbiota exhibits diurnal oscillations that influence host circadian biology.
9	(Wang et al., 2022)	Narrative review	Human and experimental studies	Circadian rhythms and gut microbiota interact to maintain metabolic balance.
10	(Franzago et al., 2023)	Review article	Nutrition and microbiome studies	Chrononutrition, diet timing, and microbial metabolites are important regulators of circadian-microbiome balance.

The selected literature demonstrates that circadian disruption influences gut microbiome regulation by altering microbial rhythmicity, functional activity, and metabolite production.

Liu et al. (2020) provided direct evidence that disruption of the sleep–wake cycle affects intestinal microbiome characteristics. In this study, healthy participants underwent an experimental sleep–wake cycle shift, and fecal microbiota analysis was performed using 16S rRNA gene sequencing. The researchers observed that circadian disturbance altered microbial functional profiles and microbial interaction networks, although substantial changes in overall bacterial composition were not detected. These findings suggest that functional microbial changes may occur earlier than measurable taxonomic dysbiosis.

The concept of microbial rhythmicity was further supported by mechanistic studies showing that gut microbiota exhibits daily oscillations influenced by feeding behavior and host circadian signals. (Daas & De Roos, 2021) explained that certain microbial populations act as "microbial oscillators" that respond to dietary timing and regulate host metabolic pathways through microbial-derived metabolites. Withrow et al. (2021) summarized evidence from human and experimental studies indicating that insufficient sleep and circadian misalignment are associated with alterations in microbial diversity and metabolite levels. Changes in short-chain fatty acids (SCFAs), secondary bile acids, and inflammatory signaling pathways are possible mechanisms linking circadian disruption to metabolic abnormalities.

Furthermore, the relationship between diet timing and microbiome regulation has become an important concept in chrononutrition. Franzago et al. (2023) emphasized that meal timing, dietary patterns, and microbial metabolites contribute to maintaining synchronization between circadian rhythms and gut microbiota. The authors highlighted that future studies should further clarify the specific microbial patterns associated with different circadian exposures.

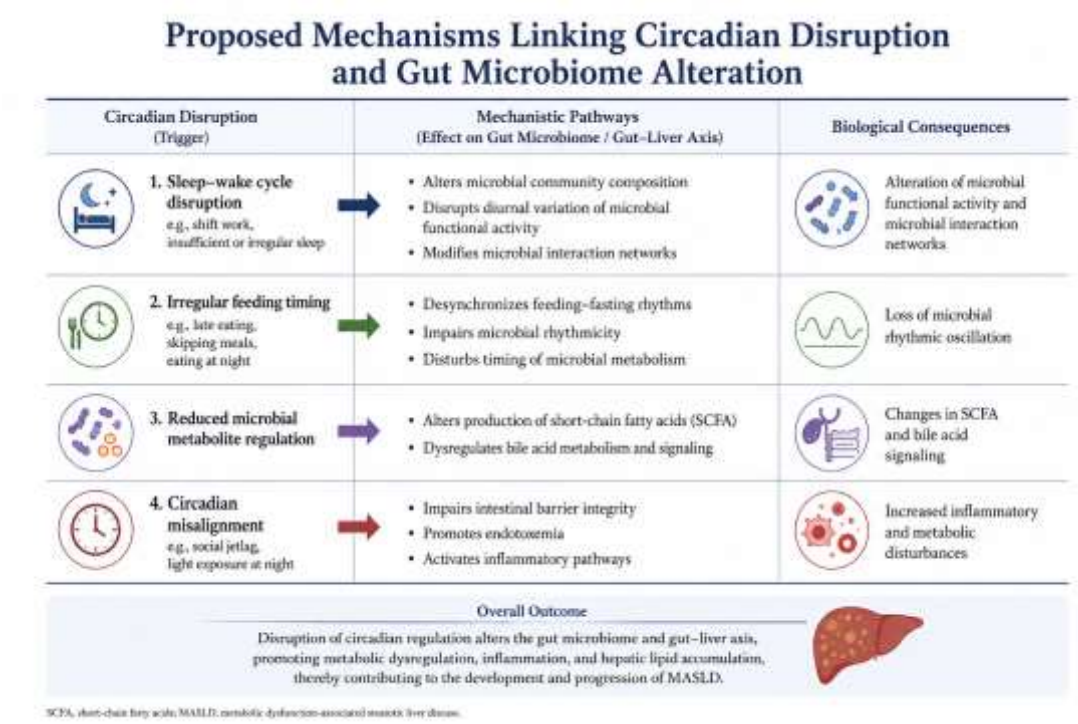

Figure 1. Proposed Mechanisms Linking Circadian Disruption and Gut Microbiome Alteration

Current evidence suggests that circadian disruption should not be considered solely as a disturbance of sleep physiology, but rather as a broader temporal disturbance affecting the interaction between the host and gut microbial ecosystem. Modern lifestyle exposures, including irregular sleep schedules, shift work, and altered meal timing, may induce circadian misalignment that subsequently disrupts normal microbial rhythmicity. These alterations may influence microbial-derived metabolites, including short-chain fatty acids, bile acid derivatives, and other signaling molecules involved in

metabolic and immune regulation. Consequently, persistent disruption of circadian–microbiome communication may contribute to metabolic and inflammatory dysregulation through microbiome-mediated mechanisms. This integrated perspective highlights the importance of considering circadian disruption as a multifactorial lifestyle-related exposure that may influence downstream metabolic disorders through alterations in host–microbial interactions.

Gut-Liver Axis: Microbial Metabolites, Bile Acid Signaling, and Hepatic Metabolic Regulation

Table 2. Characteristics of Studies Evaluating Gut-Liver Axis and Hepatic Metabolic Regulation

No	Author (Year)	Study Design	Population/Model	Main Findings Related to Gut-Liver Axis
1	(Pabst et al., 2023)	Narrative review	Human and experimental studies	Gut microbiota regulate liver homeostasis through microbial metabolites, bile acids, intestinal barrier function, and immune pathways. Dysbiosis may contribute to hepatic inflammation and metabolic dysfunction.
2	(Liu & Yang, 2023)	Review article	Experimental and translational studies	The gut-liver axis is regulated by epithelial barriers, immune signaling, microbial products, and metabolic communication between the intestine and liver.
3	(Yang et al., 2020)	Review article	Clinical liver disease studies	Gut barrier dysfunction and bacterial translocation contribute to liver inflammation via microbe-associated molecular patterns.
4	(Tilg et al., 2020)	Review article	Human metabolic studies	Alterations in the gut microbiota are associated with obesity-related metabolic dysfunction and hepatic metabolic abnormalities.

5	(Ciaula et al., 2020)	Review article	Metabolic liver disease studies	Microbiome alterations contribute to metabolic dysfunction-associated liver disease through inflammation, metabolite alterations, and immune activation.
6	(Hrncir et al., 2021)	Review article	Liver disease studies	Microbial products influence hepatic inflammation and fibrosis via immune-mediated pathways.
7	(W. Zhao et al., 2022)	Review article	NAFLD/MASLD studies	Gut microbiota-derived metabolites regulate hepatic lipid metabolism, inflammation, and disease progression in NAFLD.
8	(Liu et al., 2022)	Review article	Gut microbiome and liver metabolism studies	Microbial metabolites, including SCFAs and bile acids, act as signaling molecules that connect intestinal microbiota with hepatic metabolism.

The gut-liver axis is an essential physiological communication pathway that connects intestinal microorganisms and hepatic function. Unlike the traditional concept that considers the liver an independent metabolic organ, current evidence indicates that hepatic metabolism is strongly influenced by signals originating from the intestinal microbiota. The liver receives microbe-derived molecules directly through portal circulation, allowing intestinal microorganisms to influence hepatic metabolism, inflammation, and immune responses. Therefore, alterations in gut microbial composition may affect liver physiology through multiple mechanisms, including changes in microbial metabolites, intestinal permeability, and immune activation.

Pabst et al. (2023) emphasized that gut microbiota contributes to liver homeostasis through several interconnected pathways. Microbial metabolites, bile acid transformation, and intestinal barrier regulation represent major mechanisms through which intestinal microorganisms regulate hepatic metabolic processes. One of the major mechanisms underlying gut-liver communication involves the production and regulation of microbial-derived metabolites. Intestinal microorganisms generate various bioactive compounds that influence hepatic physiology through portal circulation, immune signaling pathways, and metabolic regulation. Among these metabolites, short-chain fatty acids (SCFAs) represent important mediators produced through bacterial fermentation of dietary fibers. SCFAs contribute to maintaining intestinal epithelial integrity, regulating immune responses, modulating glucose metabolism, and influencing hepatic energy balance. Alterations in gut

microbiota composition and function may disturb SCFA production, thereby affecting metabolic pathways involved in liver homeostasis.

In addition to SCFAs, bile acid signaling represents another critical pathway connecting intestinal microbiota with hepatic metabolism. Primary bile acids synthesized by hepatocytes are modified by intestinal bacteria into secondary bile acids, which subsequently act as signaling molecules that regulate host metabolic processes. These microbial-modified bile acids influence metabolism through nuclear and membrane receptors, including the farnesoid X receptor (FXR) and Takeda G protein-coupled receptor 5 (TGR5). Changes in gut microbial composition may alter bile acid transformation and signaling activity, potentially affecting lipid metabolism, glucose homeostasis, and inflammatory regulation within the liver.

The integrity of the intestinal barrier represents an essential component in maintaining balanced communication between the gut and liver. Under physiological conditions, the intestinal barrier limits excessive translocation of microbial products into systemic circulation. However, alterations in gut microbiota composition and intestinal permeability may increase exposure of the liver to microbial-derived molecules, including lipopolysaccharide (LPS). Yang et al. (2020) described that increased intestinal permeability facilitates bacterial component translocation through the portal circulation, resulting in the activation of hepatic inflammatory pathways. This mechanism highlights that gut microbiome disturbances may influence hepatic metabolic regulation through immune-mediated processes and contribute to liver dysfunction before the development of advanced hepatic disease.

Although most studies investigating the gut-liver axis have not directly focused on circadian disruption, this biological framework provides a plausible mechanism by which lifestyle-related circadian disturbances may influence the metabolic health of the liver. Circadian misalignment caused by irregular sleep schedules, shift work, and altered meal timing may affect several components involved in gut-liver communication, including feeding–fasting rhythms, microbial oscillations, bile acid metabolism, and hepatic lipid metabolism. Disruption of these interconnected processes may impair the synchronization between intestinal microbial activity and host metabolic requirements, thereby influencing liver metabolism and homeostasis. Therefore, the gut-liver axis may represent an important intermediary pathway linking modern lifestyle-related circadian disruption to metabolic alterations in the hepatic function.

Previous studies have frequently examined liver disease, gut microbiome alterations, and metabolic dysfunction as separate biological phenomena. However, emerging evidence supports a more integrated perspective, in which the gut-liver axis functions as a central communication pathway connecting lifestyle-related circadian disruption with hepatic metabolic regulation. Through alterations in feeding rhythms, microbial composition, microbial-derived metabolites, bile acid signaling, and inflammatory pathways, circadian disturbances may indirectly influence hepatic metabolism by changes in intestinal microbial ecology. This framework emphasizes that metabolic liver health is not determined solely by hepatic factors but is also influenced by

complex interactions between biological timing, intestinal microorganisms, and host metabolic regulation.

Circadian Disruption, Inflammation, and Metabolic Liver Health

Circadian disruption has increasingly been recognized as an important regulator of inflammatory processes involved in metabolic disorders. The circadian system not only controls sleep–wake cycles but also regulates immune activity, cytokine production, oxidative responses, and metabolic adaptation. Disturbance of circadian alignment caused by irregular sleep schedules, shift work, and altered feeding patterns may interfere with normal inflammatory regulation and contribute to metabolic imbalance. The liver is a major peripheral organ controlled by circadian regulation. Hepatic clock genes coordinate multiple physiological processes, including lipid metabolism, glucose homeostasis, oxidative stress responses, and inflammatory signaling. Therefore, disruption of circadian timing may alter hepatic metabolic pathways and increase susceptibility to inflammatory metabolic disturbances.

Table 3. Studies Evaluating Circadian Regulation, Inflammation, and Metabolic Liver Health

No	Author (Year)	Study Design	Model/Population	Main Findings
1	(Murakami & Tognini, 2020)	Literature review	Human and experimental evidence	Circadian misalignment and gut microbiota interact bidirectionally, influencing the microbial function, inflammatory pathways, and metabolic disorders.
2	(Liu et al., 2020)	Human experimental study	22 healthy adults	Sleep–wake cycle disruption alters gut microbiome functional profiles and microbial interaction networks, particularly affecting microbial functional pathways related to metabolism.

3	(Pearson et al., 2020)	Narrative review	Human and animal evidence	Circadian rhythms regulate microbial oscillations, whereas microbiota-derived signals influence host metabolism and disease susceptibility.
4	(Yang et al., 2020)	Review article	Clinical liver disease studies	Gut barrier dysfunction and bacterial translocation contribute to hepatic inflammation via microbe-associated molecular patterns and immune activation.
5	(Tilg et al., 2020)	Review article	Human metabolic studies	Alterations in the gut microbiota contribute to metabolic inflammation and hepatic metabolic abnormalities through microbial imbalance and altered signaling pathways.
6	(Withrow et al., 2021)	Narrative review	Human and non-human studies	Sleep deficiency and circadian disruption modify microbial diversity, metabolite production, and inflammatory pathways involved in metabolic regulation.
7	(Daas & De Roos, 2021)	Mechanistic review	Microbiome experimental studies	The gut microbiota mediates the relationship between dietary timing and host circadian metabolism through microbial

				metabolites and metabolic signaling.
8	(Liu et al., 2022)	Review article	Gut microbiome and liver metabolism studies	Microbial metabolites, including SCFAs and bile acids, function as signaling molecules that connect intestinal microbiota with hepatic metabolism.

The liver contains an intrinsic circadian clock that regulates metabolic pathways throughout the day. Murakami & Tognini (2020) explained that circadian regulation controls the transcriptional programs involved in glucose metabolism, lipid synthesis, mitochondrial activity, and energy utilization. When circadian alignment is disrupted, the temporal organization of these pathways may become impaired. This condition can result in the inappropriate activation of metabolic pathways, including increased lipid accumulation, impaired glucose regulation, and altered inflammatory responses.

Liu et al. (2020) emphasized that circadian disruption is an important contributor to metabolic diseases because peripheral clock dysfunction reduces the ability of metabolic organs to adapt to environmental signals. Factors such as irregular meal timing and sleep disruption may weaken the synchronization between the central circadian clock and peripheral organs, including the liver. The interaction between circadian disruption and inflammatory regulation is closely associated with gut-liver communication. Circadian misalignment caused by irregular sleep patterns, shift work, and altered feeding schedules may influence gut microbiota composition and microbial metabolic activity. These alterations can disrupt intestinal barrier integrity and increase the exposure of hepatic tissue to microbial-derived molecules through portal circulation. Consequently, changes in gut microbial ecology may contribute to the activation of hepatic inflammatory responses and metabolic disturbances.

Pearson et al., (2020) described that impaired intestinal barrier function may facilitate the translocation of microbial components, including lipopolysaccharide (LPS), into the portal circulation. Once reaching the liver, these microbial-associated molecules can activate innate immune pathways through pattern recognition receptors, leading to inflammatory signaling, cytokine production, and metabolic alterations. This mechanism provides an important explanation for how intestinal dysbiosis may influence hepatic physiology through immune-mediated pathways. Furthermore, Hsu and Schnabl (2023) emphasized that gut microbiota-derived metabolites contribute to hepatic immune regulation through several interconnected mechanisms, including microbial metabolite signaling, bile acid metabolism, intestinal barrier maintenance, and modulation of immune cell activity. Therefore, inflammation represents a critical biological link connecting gut microbiome alterations with hepatic metabolic regulation.

Microbial metabolites are important signaling molecules that mediate communication between intestinal microorganisms and systemic metabolic processes. Among these metabolites, short-chain fatty acids (SCFAs), including acetate, propionate, and butyrate, play essential roles in maintaining intestinal epithelial integrity, regulating immune balance, controlling inflammatory responses, and influencing host metabolic signaling pathways. Adequate SCFA production of SCFAs contributes to the preservation of intestinal barrier function and prevention of excessive inflammatory activation. Conversely, alterations in gut microbiota composition associated with circadian disruption or dietary imbalance may reduce the production of beneficial microbial metabolites, resulting in impaired barrier function and increased susceptibility to inflammation.

In addition to SCFAs, bacterial components such as lipopolysaccharides (LPS) are important mediators of microbiota-associated inflammation. Increased intestinal permeability allows LPS and other microbial products to enter the circulation and reach the liver, where they activate inflammatory pathways through innate immune receptors, particularly toll-like receptor signaling. The activation of these pathways promotes cytokine release, oxidative stress responses, and hepatic inflammatory processes. This mechanism is particularly relevant in metabolic liver disorders, which are characterized by persistent, low-grade inflammation, altered lipid metabolism, and progressive disruption of hepatic homeostasis. Therefore, microbial metabolites and bacterial-derived molecules are key intermediaries linking gut microbiome disturbances with inflammatory regulation and metabolic liver alterations.

Modern lifestyle patterns expose individuals to multiple simultaneous circadian stressors that may disrupt the synchronization between biological rhythms and environmental requirements. Night shift work represents one of the strongest circadian challenges because it creates a mismatch between the endogenous biological clock and externally imposed behavioral schedules, particularly affecting sleep timing, hormonal regulation, and metabolism. In addition, late-night eating may disturb the peripheral metabolic clocks located in organs such as the liver and gastrointestinal tract, as feeding time represents an important zeitgeber that regulates metabolic rhythmicity. Sleep restriction may further contribute to impaired inflammatory regulation by altering the immune responses and metabolic signaling pathways. Similarly, prolonged exposure to artificial light at night can suppress normal circadian signaling by disrupting melatonin secretion and central clock regulation. These lifestyle-related factors rarely occur independently; instead, they interact through overlapping biological pathways that influence gut microbiome regulation, inflammation, and metabolic health.

Based on the reviewed evidence, circadian disruption may be understood as an upstream lifestyle-related factor that influences metabolic regulation through interconnected interactions between biological timing, the gut microbiota, immune responses, and hepatic function. Modern lifestyle exposures, including shift work, irregular sleep patterns, artificial light exposure at night, and inconsistent meal timing, may induce circadian misalignment between endogenous biological rhythms and external behavioral schedules. This misalignment can subsequently disrupt normal sleep–wake cycles and feeding rhythms, which are important regulators of peripheral clocks and intestinal microbial oscillations.

Alterations in circadian timing may affect the composition and functional activity of the gut microbiome, leading to disturbances in microbial rhythmicity and changes in the production of microbe-derived metabolites. These alterations may influence intestinal barrier integrity, microbial metabolite signaling, and bile acid metabolism, thereby modifying communication between the intestine and liver through the gut-liver axis. Increased intestinal permeability and altered microbial signaling may promote inflammatory activation through exposure to microbe-associated molecules and immune pathway stimulation. Consequently, persistent disruption of circadian–microbiome interactions may contribute to altered hepatic metabolic regulation through the combined effects of inflammation, metabolic signaling, and liver homeostasis.

Previous studies have commonly investigated circadian disruption, gut microbiome alterations, inflammation, and hepatic metabolic disorders as separate biological processes. However, this narrative review integrates these components into a unified framework, in which circadian disruption functions as an upstream environmental and behavioral exposure that influences inflammatory regulation and hepatic metabolism through the gut-liver axis. This perspective emphasizes that metabolic liver alterations associated with modern lifestyles may not result from isolated dietary factors or individual metabolic abnormalities alone, but rather from cumulative disturbances involving biological timing, microbial ecosystem regulation, and host immune responses. Understanding these interconnected mechanisms may provide a broader perspective for identifying lifestyle-related factors that influence long-term metabolic liver health.

CONCLUSIONS AND RECOMMENDATIONS

Current evidence indicates that circadian disruption associated with modern lifestyle patterns may influence metabolic health through complex interactions between circadian regulation, gut microbiome dynamics, and gut-liver communication. Irregular sleep schedules, shift work, social jetlag, and inconsistent meal timing may disturb microbial rhythmicity, alter microbial-derived metabolites, regulate inflammation, and affect hepatic metabolic processes. The gut-liver axis provides an important framework for understanding how lifestyle-related circadian misalignment may influence gastrointestinal and hepatic health through interconnected metabolic and immune pathways.

Although current evidence supports an important relationship between circadian disruption, gut microbiome alterations, and metabolic liver regulation, further studies are required to clarify the underlying mechanisms and establish stronger causal associations. Preventive approaches may focus on maintaining regular sleep–wake patterns, optimizing meal timing, and reducing prolonged exposure to circadian misalignment through healthier lifestyles and occupational strategies. A better understanding of circadian–microbiome interactions may contribute to the development of more integrated approaches for maintaining long-term metabolic health.

ADVANCED RESEARCH

Future research should focus on improving the understanding of how chronic circadian disruption influences gut microbiome function and hepatic metabolic regulation in human populations. Current evidence is limited by differences in study design, variation in circadian exposure assessment, and the predominance of observational or experimental models with relatively short intervention periods. Future investigations should incorporate larger multicenter cohorts, longitudinal study designs, and comprehensive biological assessments.

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