


Review

The Impact of Exercise and the Potential Role of Exerkine Irisin on Sleep Quality: A Review

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Background

Physical activity has been shown to positively affect sleep performance and is increasingly acknowledged as an evidence-based, non-pharmacologic intervention for insomnia. Physically active individuals report better sleep quality, fewer sleep disorders, and reduced daytime fatigue and sleepiness.

Objective

This review provides an overview of different physical therapies to improve sleep quality in patients with insomnia. It seeks to understand whether irisin, a molecular mediator of exercise, may be involved in improving sleep quality. This article examines the documented impact of exercise on sleep quality and the possible involvement of myokine irisin.

Conclusion

Based on the literature reviewed, exercise appears to be a promising non-pharmacological option for treating insomnia and improving sleep quality in adults. Overall, current data indicate that irisin, produced during physical activity, may be one of the molecular mediators involved in this process. However, further studies are needed to better clarify its specific regulatory role on sleep.

1. INTRODUCTION

Insomnia is defined as difficulty in sleep initiation and/or maintenance and is often considered within the spectrum of psychosomatic disorders. A clinical diagnosis requires the presence of significant daytime discomfort resulting from these sleep difficulties occurring at least three nights per week, for a minimum duration of 3 consecutive months.^{1,2} Insomnia is characterized by decreased cognitive performance, fatigue, and altered mood, and may present as a primary condition or alongside high rates of comorbidity with illnesses such as cancer, hypertension, and psychiatric conditions, including anxiety and depression.² Sleep quality is a pivotal parameter for evaluating the severity of insomnia and is assessed in conjunction with onset latency, duration, and efficiency of sleep. Methods of measuring sleep quality can be categorized as subjective or objective. Among subjective tools, the widely used Pittsburgh Sleep Quality Index provides a measure of overall sleep quality through sleep parameters such as latency, duration, habitual efficiency,

and disturbances. The Insomnia Severity Index is a reliable instrument used to measure insomnia severity. A total score of 8 or higher indicates some level of insomnia, scores ranging from 15 to 21 denote moderate insomnia, while values between 22 and 28 suggest severe insomnia.³ Objective measures, such as polysomnography, provide the most complete and accurate information on the architecture and distribution of sleep phases, including total sleep time, sleep efficiency, and wake time after sleep onset.^{4,5}

Interestingly, studies excluding pharmacological therapy for insomnia have increased in recent years, highlighting the beneficial effects of exercise on sleep quality, psychological well-being, and immune function in various populations, including those with chronic primary insomnia. Ezati *et al.*⁶ reported that an 8-week aerobic exercise intervention improved all components of sleep, with significant changes in sleep duration occurring after 4 weeks. Increasing exercise intensity from mild-to-moderate enhanced all components of sleep quality, and aerobic exercise reduced total fatigue scores, even during midterm time-points between

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4 and 8 weeks of intervention.⁶ Similarly, other studies have revealed that early evening exercise can improve sleep quality,⁷ and moderate evening physical exercise may beneficially influence sleep.⁸ However, further investigation is needed to study the influence of exercise performed at different times of day on sleep quality.

In addition, aerobic exercise training has demonstrated antidepressant effects, mediated by nightly increases in non-rapid eye movement (NREM) sleep, decreases in REM sleep, and alterations of slow-wave sleep through elevated body temperature.^{6,9} Studies have also shown a significant increase in total sleep duration, efficiency, and onset latency after 6 months of aerobic training, as well as reduced awake time after sleep onset and REM latency in patients with chronic primary insomnia.¹⁰ Aerobic exercise led to a reduction in Beck Depression Inventory and Profile of Mood States scores and an increase in Rosenberg Self-Esteem Scale scores in patients with chronic primary insomnia, demonstrating a strong impact on psychological well-being.¹⁰ Furthermore, Singh *et al.*¹¹ observed a decrease in subjective sleep quality and depression in depressed individuals with insomnia after a 10-week randomized controlled trial of a supervised weight-training program conducted 3 times a week.¹¹

A significant finding from related studies indicates that aerobic training improved immune function among patients with chronic primary insomnia. Woods *et al.*¹² reported that a 6-month program of supervised aerobic exercise, consisting of 30-min brisk walking sessions 3 times per week, enhanced T-cell proliferation in previously sedentary older adults,¹² while Karacabey *et al.*¹³ concluded that regular and moderate aerobic training exerted beneficial effects on the immune system by increasing immunoglobulin (Ig) levels (IgA, IgG, and IgM).¹³ Buyukyazi *et al.*¹⁴ similarly reported higher baseline levels in natural killer cell percentages and serum IgA and IgM concentrations among elderly male athletes performing regular aerobic exercise.^{10,14}

The study by King *et al.*¹⁵ showed that moderate-intensity resistance exercise can have positive effects on various aspects of sleep quality, such as the transition from stage 1 to stage 2 sleep and a reduction in the number of awakenings during this stage.¹⁵ Reid *et al.*¹⁵ further demonstrated that a 6-week program of moderate aerobic training and sleep hygiene education was effective in improving self-reported sleep quality, mood, and quality of life in older individuals with insomnia, with an increase in sleep duration of 1.25 h, higher than what has been reported for other non-pharmacological treatments.^{12,16}

2. CIRCADIAN RHYTHMS AND INSOMNIA

Circadian rhythms are intrinsic, approximately 24-h cycles in physiological and behavioral processes, regulated by endogenous molecular clocks. The master circadian pacemaker in mammals is in the suprachiasmatic nucleus (SCN) of the hypothalamus, which synchronizes peripheral clocks throughout the body.^{17,18} These rhythms play a fundamental role in regulating the sleep–wake cycle, hormone secretion, metabolism, and mood.

Circadian rhythms are modulated by core clock genes, including the brain and muscle ARNT-like1 (*BMAL1*) gene. These genes establish stable circadian rhythms through transcription-translation negative feedback loops and other regulatory interactions that stabilize the system.^{19–22} Almost

all cells in the body express these clock genes, and many are capable of sustaining autonomous circadian rhythms in isolated preparations, including tissue slices and cell cultures.²³

Sleep problems are commonly considered a manifestation of circadian disruption.²³ Sleep is influenced by both homeostatic sleep pressure and circadian timing. Biological rhythms are entrained by environmental cues, especially light.²³ Disruption of the light-dark cycle alters clock gene expression in the prefrontal cortex and hippocampus, contributing to mood and behavioral disorders.²⁴

One of the population's most vulnerable to circadian disruption is shift workers. Shift work refers to any work schedule that occurs outside of the standard 7 a.m.–6 p.m. window²⁵ and includes permanent night shifts, early morning shifts, or rotating schedules, which are common in healthcare, emergency services, transport, and hospitality.²⁶ Such schedules disrupt the body's internal clock, often resulting in shortened sleep duration, increased sleep latency, and insomnia.²⁷

Another widespread form of circadian disruption is social jetlag, a discrepancy between an individual's endogenous biological rhythm and their social demands. This condition typically manifests as delayed sleep and wake times on weekends relative to weekdays and has been associated with insomnia, impaired sleep quality, and mood disorders.²⁸

3. THE POTENTIAL ROLE OF THE EXERCISE-MIMETIC IRISIN IN IMPROVING SLEEP QUALITY

Irisin is a novel exercise-induced myokine that exerts pleiotropic effects on the body's metabolism.²⁹ Several clinical studies have evaluated whether sleep disturbances affect circulating irisin levels. In a study of patients with rheumatoid arthritis, reduced concentrations of irisin were associated with poor sleep quality.³⁰ In obstructive sleep apnea (OSA), a condition characterized by disrupted sleep and often associated with obesity, decreased irisin concentrations have been observed and found to correlate inversely with disease severity.³¹ In addition, elevated irisin levels have been linked to enhanced daytime sleepiness in patients with OSA.³²

4. PRECLINICAL DATA

Recently, studies conducted on mouse models have suggested that short-term irisin treatment reduced depression- and anxiety-like behavior.³³ Since the negative relationship between anxiety and sleep quality is well-established, irisin may potentially improve sleep quality by reducing depressive and anxious behaviors. Study outcomes were derived from the forced swim test and tail suspension test, which are among the most commonly used methods for assessing depressive-like behavior and screening antidepressant drugs.³³ In both tests, the duration of immobility was recorded as an indicator of behavioral despair, which is a condition characterized by the animal's total absence of movement, including climbing, swimming, escaping, or scratching.^{34–37} The results of the investigation demonstrated that the immobility duration was significantly reduced in irisin-treated animals compared with the controls. Furthermore, in the forced swim test, the irisin-treated mice displayed pronounced swimming activity

and reduced immobility time in the short-term protocol compared with the long-term protocol (25% vs. 18%).³⁸ Long-term irisin administration also suggested a potential anxiolytic effect, as evidenced by a decreasing trend in the duration spent in the inner zone of the Open Field Test arena.³⁸ Considering that depression may be exacerbated or caused by anxiety disorders,³⁹ the effect of once-daily short-term systemic irisin administration on anxiety was also evaluated using the elevated plus maze tool. In this test, animals were placed at the intersection of the four arms of the maze, and the number of entries and duration spent in each arm were recorded. Irisin treatment significantly increased both the number of entries and the time spent in the open arms, indicating that the irisin-treated mice were more inclined to explore open spaces compared to the control group. In addition, the study showed that systemic administration of irisin, which can cross the blood-brain barrier,^{40,41} significantly increased the expression of peroxisome proliferator-activated receptor- γ coactivator 1- α (PGC-1 α) and fibronectin Type III domain-containing protein 5 (FNDC5), the precursor of irisin, in both the hippocampus and prefrontal cortex. Thus, it is plausible to hypothesize that activation of the FNDC5/irisin pathway in the brain areas primarily involved in mood regulation may contribute to the antidepressant- and anxiolytic-like effects of irisin.

Wang and Pan⁴² demonstrated that irisin levels decreased in the brains of rats exposed to chronic unpredictable stress, a widely used rodent depression model. Furthermore, they showed that subcutaneous administration of irisin for 14 days reduced chronic unpredictable stress-induced behavioral deficits by modulating energy metabolism in the prefrontal cortex.⁴² Similarly, Siteneski *et al.*⁴³ demonstrated that irisin, when injected directly into the cerebral lateral ventricles, reduced depressive-like behaviors in young healthy male mice subjected to stress situations. This effect was attributed to the modulation of brain gene expression, including brain-derived neurotrophic factor (*BDNF*), *PGC-1 α* , and *FNDC5*.⁴³ However, further investigations are needed to better clarify the molecular mechanisms through which irisin influences depression- and anxiety-like behaviors, as well as its potential role in improving sleep in humans.⁴⁴

In a separate cardiac ischemia-reperfusion model, melatonin administration conferred cardioprotection by reducing oxidative stress and inflammation while also increasing mRNA expression of cardiac irisin.⁴⁵⁻⁴⁷

Further mechanistic insight was provided by Ouyang *et al.*,⁴⁸ who demonstrated that combining melatonin and irisin produced additive improvement in cardiac function by suppressing a pathway implicated in cellular apoptosis and oxidative injury.⁴⁹ These converging findings underscore irisin's role as a downstream effector of melatonin across multiple physiological systems.

Building on these interactions, recent evidence highlights the broader coordination of melatonin, exercise, and irisin. Exercise activates the BMAL1-PGC-1 α -FNDC5 axis, promoting irisin release and linking muscle activity with mitochondrial regulation, circadian signaling, and thermogenesis.^{50,51} Melatonin reinforces this signaling by modulating *BMAL1* and peripheral clock genes, thereby amplifying irisin's effects in metabolic tissues. Moreover, irisin stimulates *BDNF* expression, enhancing synaptic plasticity and neurogenesis—effects shared by melatonin in central nervous and chronobiological domains.^{42,52} These intersecting pathways suggest that melatonin and exercise may co-regulate irisin's endocrine

and neuromodulatory roles, promoting homeostasis at molecular, systemic, and behavioral levels. While direct tri-directional feedback between these agents remains under-characterized, existing data strongly support their mutual reinforcement through overlapping transcriptional and signaling networks.

5. EXERCISE MODALITIES AND THEIR IMPACT ON SLEEP

5.1. YOGA

Yoga is an ancient Eastern discipline that originated in India. Conventionally, Indian yoga integrates multiple domains—including ethical principles, physical postures, and spiritual practices—aimed at harmonizing mind and body, enhancing mental well-being, and fostering self-awareness.^{53,54} A yoga trial involving breast cancer survivors with chronic fatigue demonstrated that yoga was safe and effective in improving fatigue severity, depression, and sleep quality.⁵⁵ There is growing evidence that yoga can help to reduce the negative effects of cancer treatment, such as fatigue, anxiety, and sleep difficulties.⁵⁶⁻⁵⁸ In a meta-analysis that examined the effects of yoga intervention on sleep in breast cancer patients,⁵⁹ it significantly increased sleep quality. In a study by Carson *et al.*,⁶⁰ a group-based yoga intervention, consisting of 120-min sessions once per week, reduced the frequency of sleep disturbances after 1 month.⁶⁰ More recent studies reported that individualized yoga interventions—60 min, 3 times per week—can improve sleep-related scores on the European Organization for Research and Treatment of Cancer Quality-of-Life Questionnaire-Core 30 after 8 weeks.⁵⁹ Similar results were reported by Yagli and Yulger⁶¹ and Rao *et al.*,⁶² whose studies concluded that yoga reduces fatigue, depression, and pain, while supporting routine functioning and improving quality of life in cancer patients.^{61,62} A clinical trial reported significant improvements in insomnia and sleep parameters—such as reduced wake time after sleep onset and improved sleep efficiency—in individuals undergoing a yoga program.⁵⁸ Moreover, yoga participants reduced their use of sleep medication by 21%, while control participants showed a 5% increase.⁵⁸

A systematic review and meta-analysis by Wang *et al.*⁶³ demonstrated that yoga intervention offers benefits over non-active controls in managing sleep disturbance.⁶³ Only one study has examined the impact of yoga training on irisin levels. Conducted in obese adults aged 40–50, the study found that yoga significantly increased circulating irisin levels compared to a non-trained control group.⁶⁴

5.2. TAI CHI

Tai chi is an ancient martial art that combines physical movements with relaxation techniques. It originated during the late Ming and early Qing Dynasties and has since gained global popularity, with over 5 million practitioners in the United States alone.⁶⁵ Increasing evidence highlights the beneficial effects of tai chi on sleep quality and insomnia. A meta-analysis by Han *et al.*⁶⁶ highlighted that tai chi significantly improved insomnia symptoms compared to exercise and health education alone. Subgroup analyses suggested it was as effective as cognitive behavioral therapy.⁶⁷ Similarly, another meta-analysis focusing on university students reported that tai chi enhanced sleep quality,

although general aerobic exercise had a slightly greater effect.⁶⁸

Vanderlinden *et al.*⁶⁹ reported a higher proportion of participants achieving good sleep in tai chi groups compared to those performing other single exercise types, such as yoga, brisk walking, pilates, or cycling.⁶⁹ These results support tai chi as an effective exercise modality for enhancing sleep quality, particularly in older populations.

A recent prospective clinical study evaluated the impact of tai chi on irisin levels and cognitive performance. The results showed a significant increase in irisin levels in the tai chi group over 6 months, in comparison with a non-exercising control group. Moreover, in the tai chi group at 6 months, irisin levels correlated significantly with scores on the Auditory Verbal Learning Test-Delayed, a measure of memory function.⁷⁰

However, despite its established benefits, findings from tai chi studies vary due to participant demographics (e.g., country or region) and differences in style, intervention duration, frequency, and intensity.⁷¹ Further research is needed to deepen our knowledge of how these factors influence tai chi's effectiveness in improving sleep quality among different populations.

5.3. RESISTANT TRAINING

Resistance training (RT) has been investigated for its potential to improve sleep quality and alleviate anxiety. Nine sessions of high-intensity RT conducted over 3 weeks significantly improved both sleep quality and anxiety symptoms compared to a control group.⁷² RT is known to improve muscle strength and function and may also reduce inflammation and enhance sleep parameters across various age groups.⁷³

Studies on cancer patients have yielded mixed results. Langlais *et al.*⁷⁴ reported a beneficial effect of RT (−11.1%) in men with metastatic castration-resistant prostate cancer who participated in a combined aerobic and resistance exercise pilot intervention.⁷⁴ Another study observed no improvement in the intervention group, although the control group experienced a decline in sleep quality.⁷⁵ A third study, involving prostate cancer patients undergoing radiotherapy, found that RT had a negative impact on sleep quality (12.5%).⁷⁶ However, the average percentage difference across studies still suggested that RT may improve sleep quality (+0.3%) compared with the control groups (+8.1%).⁷⁷

A previous systematic review suggested that RT could improve sleep quality, though it included heterogeneous populations and excluded cancer survivors, who may experience more severe sleep disturbances.⁷⁸ Notably, only three studies assessed sleep quality using the Pittsburgh Sleep Quality Index; however, with mixed results.⁷⁴⁻⁷⁶

To explore potential mechanisms, one study investigated the effects of sleep deprivation-induced muscle atrophy in rats that had previously undergone RT.⁷⁹ The study found that sleep deprivation caused muscle atrophy, likely due to elevated corticosterone and catabolic signaling. However, high-intensity RT performed beforehand helped reduce muscle loss.⁷⁹

A study conducted in aging mice and humans found that circulating irisin levels increased alongside improvements in muscle strength following RT. In mice, irisin expression in the soleus muscle increased after 12 weeks of training. Similarly, in elderly humans, greater muscle strength was positively correlated with higher circulating irisin levels.⁸⁰

A systematic review and meta-analysis examined the effects of chronic RT on circulating irisin in adults. It included

randomized controlled trials measuring irisin levels after endurance training programs lasting at least 8 weeks. While the overall analysis of 282 individuals showed a non-significant trend toward increased irisin levels, subgroup analyses revealed significant increases in older adults, particularly when the training program was progressively intensified.⁸¹

While these studies suggest that irisin may enhance muscle function and physical well-being after RT, its role in sleep promotion remains underexplored. In the context of acute exercise, irisin has been shown to stimulate *BDNF* expression in the hippocampus.⁴¹ Likewise, another study has demonstrated that *BDNF* injected into the rat brain during wakefulness enhanced the depth of subsequent non-REM sleep.⁸² These results indicate that improved sleep quality following RT may be partially mediated by irisin-induced *BDNF* expression. However, it remains unclear whether centrally or peripherally induced increases in irisin signaling can directly enhance sleep. Future mechanistic studies, in animal models treated with irisin and subjected to RT and/or sleep deprivation, could provide valuable insights into the role of this myokine in RT-mediated sleep effects.

6. TIME AND CONSISTENCY OF PHYSICAL EXERCISE IN SLEEP QUALITY

An increasing number of studies have investigated the effects of late evening exercise, particularly whether it negatively affects sleep. Several findings suggest that evening exercise can positively influence sleep, provided it is not performed too close to bedtime. However, a systematic review and meta-analysis found that acute evening exercise performed before bedtime does not disturb nighttime sleep in healthy, well-trained adults without sleep disorders.⁸⁵ Specifically, high-intensity exercise performed 2 h before bedtime improved sleep, while intense exercise ending just 1 h before bedtime delayed sleep onset and decreased sleep duration. In addition, among sedentary individuals, a single session of intense exercise induced positive changes in nighttime sleep, stimulating sleep onset and lengthening sleep duration.⁸³

In addition to influencing irisin levels, physical activity may serve as a non-photocircadian synchronizer, also known as a zeitgeber. Zeitgebers are external cues that synchronize the body's internal biological clocks with the 24-h light-dark cycle. While light remains the dominant zeitgeber, appropriately timed exercise can also shift circadian phase and stabilize rhythm amplitude. Physical activity may stabilize the circadian system through feedback mechanisms involving the SCN—the brain's master clock. Regular exercise helps to maintain high-amplitude circadian rhythms, particularly by supporting clock gene expression in the SCN.⁸⁴

For example, morning exercise tends to promote phase advancement—leading to earlier sleep onset—while late evening exercise may delay circadian phase depending on its intensity and timing. As such, it may be less beneficial for sleep.⁸⁵⁻⁹⁰ The overall benefits of exercise timing may vary depending on an individual's chronotype.⁸⁴ Thus, exercise not only directly affects sleep architecture but also indirectly through circadian regulation. This temporal sensitivity suggests that optimal sleep outcomes may depend on personalized timing of exercise.⁸⁴ Understanding these mechanisms is particularly relevant for individuals with circadian rhythm disorders, such as shift workers or those with delayed sleep phase syndrome.⁸⁴ Future studies should investigate

how chronotype and habitual activity timing influence the circadian and sleep-enhancing effects of exercise.

Concerning the involvement of irisin in physical activity, based on the time of practice, it has been shown that day-night fluctuation can influence its synthesis in humans. Anastasilakis *et al.*⁹¹ analyzed 122 young, healthy individuals exposed to a standard day-night cycle, who performed 30-min aerobic exercise under controlled nutritional conditions. They reported a clear circadian rhythm in irisin secretion, with peak levels occurring around 9:00 p.m. and the lowest early in the morning.⁹¹ Notably, the diurnal rhythm of circulating irisin followed an inverse pattern to serum cortisol levels, with no significant gender difference observed. Irisin levels were unaffected by dietary habits, but increased acutely following a 30-min aerobic exercise.⁹¹ A key strength of the study—which was the first to highlight the circadian rhythm of irisin secretion—was its relatively large, homogeneous sample of healthy individuals with similar age and body mass index.⁹¹ However, future studies are needed to demonstrate if and how exercise timing modulates irisin's diurnal rhythm. Such investigations could help clarify whether evening peaks in irisin levels are predictive of its sleep-modulating effects.

Another unanswered question is whether the positive impact of exercise on sleep persists over time. While enhancement in sleep quality has been noted during post-intervention periods, results remain highly heterogeneous. A systematic review and meta-analysis of randomized controlled trials found that aerobic exercise increased sleep in cancer patients with sleep difficulties, and these benefits were still evident at 3–6 months post-intervention.⁹² However, high heterogeneity was reported at the post-intervention time point, and meta-regression analyses failed to identify the contributing factors.⁹² These persistent effects, along with the unexplained heterogeneity, highlight the need for further research into factors that influence the long-term impact of exercise on sleep quality.

Before discussing how exercise timing affects sleep, it is important to consider the circadian regulation of key exercise-related molecules, such as irisin. Irisin expression is regulated by circadian rhythms. The master clock, located in the SCN of the hypothalamus, synchronizes peripheral cellular clocks to maintain internal temporal homeostasis.⁹³ Among these peripheral mechanisms, the BMAL1-PGC-1 α -FNDC5/irisin axis has emerged as a key pathway linking circadian timing to metabolic adaptations. FNDC5/irisin expression follows a circadian rhythm that is transcriptionally driven by the core clock gene *BMAL1* and the muscle-specific coactivator PGC-1 α .^{94–97}

BMAL1 stimulates *FNDC5* transcription in a manner proportional to its concentration by binding to E-box motifs in the *FNDC5* promoter. Overexpression of *BMAL1* significantly increases FNDC5/irisin levels, whereas its silencing leads to their suppression.^{98–101} This finding has been confirmed in human plasma samples, where participants in the evening group had significantly higher irisin concentration than those in the morning group following an RT protocol. Similarly, muscle FNDC5/irisin levels exhibit circadian rhythmicity in mammals, in agreement with findings that show strength and training adaptations tend to be greater in the evening.^{50,102–104}

Taken together, the BMAL1-PGC-1 α -FNDC5/irisin axis represents a central molecular mechanism through which circadian timing modulates training outcomes and systemic energy regulation.⁹³

7. GENDER DIFFERENCE IN SLEEP QUALITY

Sex-based differences in sleep disorders have been widely reported across clinical and epidemiological studies. Insomnia is approximately 1.4 times more prevalent in women than in men.¹⁰⁵ Female populations throughout certain stages in their life span may be more susceptible to insomnia. Hormonal changes—particularly involving follicle-stimulating hormones, luteinizing hormones, and progesterone—may significantly influence women's sleep patterns¹⁰⁶, especially during adolescence,¹⁰⁷ pregnancy, postpartum period,¹⁰⁸ or menopause phase. Elevated levels of estrogen and progesterone, especially during the early luteal phase, have been linked with increased wakefulness and impaired sleep quality.¹⁰⁹ Estrogen and progesterone influence neurochemical transmission by enhancing wake-promoting pathways and suppressing sleep-promoting neurotransmitters.¹¹⁰ Despite recent insights from Andersen *et al.*¹¹¹ on the effect of hormonal fluctuations on sleep in women, there remains a lack of studies exploring how physical activity interventions can be tailored to hormonal cycles to optimize sleep outcomes.

Moreover, challenges such as assessing hormone levels throughout the menstrual cycle and the prevalence of gynecological conditions—such as endometriosis, dysmenorrhea, and abnormal uterine bleeding—make it difficult to assess their combined impact on sleep quality in women with insomnia.

Exercise-related sleep outcomes also differ across age groups. For example, a meta-analysis by Rubio-Arias *et al.*¹¹² found that aerobic exercise improved sleep quality in middle-aged women.¹¹² Similarly, another meta-analysis revealed that programmed aerobic exercise improved the sleep quality of pregnant women.¹¹³ Interestingly, the comparative effectiveness of aerobic exercise versus general exercise was minimal, and opposite trends emerged in middle-aged pregnant women, suggesting that certain exercise modalities may affect this group differently.^{112,113}

While aerobic exercise is generally considered the most effective for enhancing sleep quality, the potential superiority of lower-intensity modalities—such as yoga, tai chi, and relaxation training—especially in pregnant women, warrants further investigation.¹¹³ The impact of yoga on sleep quality and insomnia in women may also vary by age. A systematic review indicated that yoga did not improve insomnia severity in peri- and postmenopausal women.^{63,112}

These gender- and age-related variations in response to exercise highlight the need for further research to determine which modalities and intensities are the most effective in enhancing sleep quality among different female populations. Moreover, with regard to a possible interaction between sex hormones and irisin, independent of the level of physical exercise, it is currently unclear whether the mechanism of irisin increase could be related to changes in estrogen and progesterone levels. It is known that in women aged between 41 and 82, irisin levels correlate negatively with age, suggesting that irisin decreases simultaneously with the reduction in estrogen levels.¹¹⁴ With greater certainty, it can only be hypothesized that the loss of muscle mass in menopausal women may be one of the reasons for the decline in irisin levels.

Importantly, both estrogen and irisin act on shared systems: they protect the bones, reduce inflammation, and influence the brain. Estrogen suppresses sleep-active ventrolateral pre-optic nucleus neurons by downregulating prostaglandin D₂,¹¹⁵ promotes sleep recovery, and

interacts with kisspeptin, neurokinin B, and dynorphin neuron networks to regulate REM and NREM sleep.¹¹⁶ These effects are complemented by irisin's influence on circadian gene expression and its shared activation of intracellular pathways.

8. METHODOLOGICAL CHALLENGES

Many studies lacked well-defined control groups, failing to establish a sufficient baseline for comparison. In several trials, control groups received interventions such as sleep education, sleep hygiene training, or group recreational activities, which may have introduced non-specific benefits of confounding variables. Alternatively, waiting list control designs may have acted as placebo conditions, in which participants anticipate negative outcomes, potentially skewing results.¹¹⁷ There is a critical need to develop more robust and standardized control conditions for sleep research.

Despite noticeable impacts observed on subjective sleep outcomes, physical exercise has not consistently demonstrated benefits on physiological sleep parameters in healthy adults. For example, a meta-analysis of 22 randomized controlled trials comprising 1806 participants found that exercise significantly improved sleep efficiency, but did not statistically significantly affect sleep onset latency, wake after sleep onset, or total sleep time.¹¹⁸ In such cases, subjective assessment tools, such as sleep questionnaires, may offer more sensitive detection of perceived improvements in sleep quality.

Although polysomnography is still considered the gold standard for objective sleep evaluation, some meta-analyses suggest combining it with subjective assessments, as actigraphy may be less reliable for detecting wake episodes.⁸⁵

9. CONCLUSION

Exercise represents a promising non-pharmacological alternative for improving sleep quality and managing insomnia in adult patients. However, more studies are necessary to address the gaps in understanding of the specific role of exercise-induced irisin on sleep. Moreover, assuming that irisin is one of the molecular mediators of exercise in enhancing sleep quality, an unanswered question still concerns the optimal time window for performing physical activity, considering the day-night rhythm of irisin secretion, with maximum levels in the evening. While aerobic exercise remains the most consistently effective modality, RT may have unique benefits in preserving muscle function under sleep deprivation and promoting irisin release. Mind-body approaches, such as yoga and tai chi, offer promising alternative interventions, especially for older individuals or those with limited mobility, with early evidence suggesting these may also moderately elevate irisin levels. However, further studies should clarify whether irisin production induced by muscle contraction to promote sleep is impaired by sleep disturbances, which are very common in today's restless lifestyle.

Future research should prioritize clarifying irisin's mechanistic role in sleep through human trials with molecular endpoints, developing chronotype-specific and

hormone-informed exercise prescriptions, standardizing measurement protocols for irisin and sleep quality, and evaluating long-term adherence and durability of effects through longitudinal designs. It will be relevant to investigate whether evening exercise, coinciding with the natural peak of irisin, results in better sleep outcomes than morning exercise, test how menstrual cycle phases influence irisin's role in sleep improvement, and examine the impact of different exercise modalities on irisin secretion patterns and sleep quality in menopausal women. A priority for future research could also be to evaluate whether combining chronotherapy and exercise potentiates irisin-related sleep benefits.

From a clinical perspective, several actionable insights emerge. Clinicians should encourage moderate-intensity aerobic exercise, such as brisk walking, for individuals with chronic insomnia, ideally 2–3 h before bedtime. For postmenopausal women, RT may be particularly beneficial by promoting sleep and preserving musculoskeletal health. For pregnant women, prenatal yoga and low-impact aerobic activity could offer both sleep and metabolic benefits.

Finally, the recommended clinical approach for people experiencing circadian rhythm disorders may benefit from activities such as evening exercise and mindfulness-based practices, such as yoga or tai chi, which can help realign the circadian rhythm and manage anxiety and insomnia.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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REFERENCES

1. Araujo T, Jarrin DC, Leanza Y, Vallieres A, Morin CM. Qualitative studies of insomnia: Current state of knowledge in the field. *Sleep Med Rev.* 2017;31:58-69. doi: [10.1016/j.smrv.2016.01.003](https://doi.org/10.1016/j.smrv.2016.01.003)
2. Morin CM, Benca R. Chronic insomnia. *Lancet.* 2012;379(9821):1129-1141. doi: [10.1016/S0140-6736\(11\)60750-2](https://doi.org/10.1016/S0140-6736(11)60750-2)
3. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ.* 1997;315(7109):629-634. doi: [10.1136/bmj.315.7109.629](https://doi.org/10.1136/bmj.315.7109.629)
4. Ibanez V, Silva J, Cauli O. A survey on sleep assessment methods. *PeerJ.* 2018;6:e4849. doi: [10.7717/peerj.4849](https://doi.org/10.7717/peerj.4849)
5. Reed DL, Sacco WP. Measuring sleep efficiency: What should the denominator be? *J Clin Sleep Med.* 2016;12(2):263-266. doi: [10.5664/jcsm.5498](https://doi.org/10.5664/jcsm.5498)
6. Ezati M, Keshavarz M, Barandouzi ZA, Montazeri A. The effect of regular aerobic exercise on sleep quality and fatigue among female student dormitory residents. *BMC Sports Sci Med Rehabil.* 2020;12:44. doi: [10.1186/s13102-020-00190-z](https://doi.org/10.1186/s13102-020-00190-z)
7. Alnawwar MA, Alraddadi MI, Algethmi RA, Salem GA, Salem MA, Alharbi AA. The effect of physical activity on sleep quality and sleep disorder: A systematic review. *Cureus.* 2023;15(8):e43595. doi: [10.7759/cureus.43595](https://doi.org/10.7759/cureus.43595)
8. Saidi O, Davenne D, Lehorgne C, Duche P. Effects of timing of moderate exercise in the evening on sleep and subsequent dietary intake in lean, young, healthy adults: Randomized crossover study. *Eur J Appl Physiol.* 2020;120(7):1551-1562. doi: [10.1007/s00421-020-04386-6](https://doi.org/10.1007/s00421-020-04386-6)
9. Park I, Diaz J, Matsumoto S, et al. Exercise improves the quality of slow-wave sleep by increasing slow-wave stability. *Sci Rep.* 2021;11(1):4410. doi: [10.1038/s41598-021-83817-6](https://doi.org/10.1038/s41598-021-83817-6)
10. Abd El-Kader SM, Al-Jiffri OH. Aerobic exercise affects sleep, psychological wellbeing and immune system parameters among subjects with chronic primary insomnia. *Afr Health Sci.* 2020;20(4):1761-1769. doi: [10.4314/ahs.v20i4.29](https://doi.org/10.4314/ahs.v20i4.29)
11. Singh NA, Clements KM, Fiatarone MA. A randomized controlled trial of the effect of exercise on sleep. *Sleep.* 1997;20(2):95-101. doi: [10.1093/sleep/20.2.95](https://doi.org/10.1093/sleep/20.2.95)
12. Woods JA, Ceddia MA, Wolters BW, Evans JK, Lu Q, McAuley E. Effects of 6 months of moderate aerobic exercise training on immune function in the elderly. *Mech Ageing Dev.* 1999;109(1):1-19. doi: [10.1016/s0047-6374\(99\)00014-7](https://doi.org/10.1016/s0047-6374(99)00014-7)
13. Karacabey K, Saygin O, Ozmerdivenli R, Zorba E, Godekmerdan A, Bulut V. The effects of exercise on the immune system and stress hormones in sports-women. *Neuro Endocrinol Lett.* 2005;26(4):361-366.
14. Buyukyazi G, Kutukculer N, Kutlu N, Genel F, Karadeniz G, Ozkutuk N. Differences in the cellular and humoral immune system between middle-aged men with different intensity and duration of physically training. *J Sports Med Phys Fitness.* 2004;44(2):207-214.
15. King AC, Pruitt LA, Woo S, et al. Effects of moderate-intensity exercise on polysomnographic and subjective sleep quality in older adults with mild to moderate sleep complaints. *J Gerontol A Biol Sci Med Sci.* 2008;63(9):997-1004. doi: [10.1093/gerona/63.9.997](https://doi.org/10.1093/gerona/63.9.997)
16. Reid KJ, Baron KG, Lu B, Naylor E, Wolfe L, Zee PC. Aerobic exercise improves self-reported sleep and quality of life in older adults with insomnia. *Sleep Med.* 2010;11(9):934-940. doi: [10.1016/j.sleep.2010.04.014](https://doi.org/10.1016/j.sleep.2010.04.014)
17. Takahashi JS, Hong HK, Ko CH, McDearmon EL. The genetics of mammalian circadian order and disorder: Implications for physiology and disease. *Nat Rev Genet.* 2008;9(10):764-775. doi: [10.1038/nrg2430](https://doi.org/10.1038/nrg2430)
18. Sinha P, Meng M. Superimposed hemifields in primary visual cortex of achiasmic individuals. *Neuron.* 2012;75(3):353-355. doi: [10.1016/j.neuron.2012.07.003](https://doi.org/10.1016/j.neuron.2012.07.003)
19. Gallego M, Virshup DM. Post-translational modifications regulate the ticking of the circadian clock. *Nat Rev Mol Cell Biol.* 2007;8(2):139-148. doi: [10.1038/nrm2106](https://doi.org/10.1038/nrm2106)
20. Gekakis N, Staknis D, Nguyen HB, et al. Role of the CLOCK protein in the mammalian circadian mechanism. *Science.* 1998;280(5369):1564-1569. doi: [10.1126/science.280.5369.1564](https://doi.org/10.1126/science.280.5369.1564)
21. van der Horst GT, Muijtjens M, Kobayashi K, et al. Mammalian Cry1 and Cry2 are essential for maintenance of circadian rhythms. *Nature.* 1999;398(6728):627-630. doi: [10.1038/19323](https://doi.org/10.1038/19323)
22. Zheng B, Albrecht U, Kaasik K, et al. Nonredundant roles of the mPer1 and mPer2 genes in the

- mammalian circadian clock. *Cell*. 2001;105(5):683-694. doi: [10.1016/s0092-8674\(01\)00380-4](https://doi.org/10.1016/s0092-8674(01)00380-4)
23. McCarthy MJ, Gottlieb JF, Gonzalez R, *et al*. Neurobiological and behavioral mechanisms of circadian rhythm disruption in bipolar disorder: A critical multi-disciplinary literature review and agenda for future research from the ISBD task force on chronobiology. *Bipolar Disord*. 2022;24(3):232-263. doi: [10.1111/bdi.13165](https://doi.org/10.1111/bdi.13165)
 24. Otsuka Y, Kaneita Y, Itani O, *et al*. The relationship between subjective happiness and sleep problems in Japanese adolescents. *Sleep Med*. 2020;69:120-126. doi: [10.1016/j.sleep.2020.01.008](https://doi.org/10.1016/j.sleep.2020.01.008)
 25. Torquati L, Mielke GI, Brown WJ, Burton NW, Kolbe-Alexander TL. Shift work and poor mental health: A meta-analysis of longitudinal studies. *Am J Public Health*. 2019;109(11):e13-e20. doi: [10.2105/AJPH.2019.305278](https://doi.org/10.2105/AJPH.2019.305278)
 26. Alterman T, Luckhaupt SE, Dahlhamer JM, Ward BW, Calvert GM. Prevalence rates of work organization characteristics among workers in the U.S.: Data from the 2010 National Health Interview Survey. *Am J Ind Med*. 2013;56(6):647-659. doi: [10.1002/ajim.22108](https://doi.org/10.1002/ajim.22108)
 27. Hawkes RE, Sugavanam T, Benton JS, *et al*. Which individually-directed non-pharmacological interventions are effective at improving sleep outcomes in shift workers? A systematic review of systematic reviews. *Sleep Med Rev*. 2025;82:102110. doi: [10.1016/j.smrv.2025.102110](https://doi.org/10.1016/j.smrv.2025.102110)
 28. Sudy AR, Ella K, Bodizs R, Kaldi K. Association of social jetlag with sleep quality and autonomic cardiac control during sleep in young healthy men. *Front Neurosci*. 2019;13:950. doi: [10.3389/fnins.2019.00950](https://doi.org/10.3389/fnins.2019.00950)
 29. Bao JF, She QY, Hu PP, Jia N, Li A. Irisin, a fascinating field in our times. *Trends Endocrinol Metab*. 2022;33(9):601-613. doi: [10.1016/j.tem.2022.06.003](https://doi.org/10.1016/j.tem.2022.06.003)
 30. Gamal RM, Mohamed ME, Hammam N, El Fetoh NA, Rashed AM, Furst DE. Preliminary study of the association of serum irisin levels with poor sleep quality in rheumatoid arthritis patients. *Sleep Med*. 2020;67:71-76. doi: [10.1016/j.sleep.2019.10.021](https://doi.org/10.1016/j.sleep.2019.10.021)
 31. Li Y, Li X, Sun D, Cai S. Association of serum irisin concentrations with the presence and severity of obstructive sleep apnea syndrome. *J Clin Lab Anal*. 2017;31(5):e22077. doi: [10.1002/jcla.22077](https://doi.org/10.1002/jcla.22077)
 32. More CE, Papp C, Harsanyi S, *et al*. Altered irisin/BDNF axis parallels excessive daytime sleepiness in obstructive sleep apnea patients. *Respir Res*. 2019;20(1):67. doi: [10.1186/s12931-019-1033-y](https://doi.org/10.1186/s12931-019-1033-y)
 33. Pignataro P, Dicarlo M, Suriano C, *et al*. Once-daily subcutaneous irisin administration mitigates depression- and anxiety-like behavior in young mice. *Int J Mol Sci*. 2023;24(7):6715. doi: [10.3390/ijms24076715](https://doi.org/10.3390/ijms24076715)
 34. Porsolt RD, Bertin A, Jalfre M. Behavioral despair in mice: A primary screening test for antidepressants. *Arch Int Pharmacodyn Ther*. 1977;229(2):327-336.
 35. Steru L, Chermat R, Thierry B, Simon P. The tail suspension test: A new method for screening antidepressants in mice. *Psychopharmacology (Berl)*. 1985;85(3):367-370. doi: [10.1007/BF00428203](https://doi.org/10.1007/BF00428203)
 36. Can A, Dao DT, Terrillion CE, Piantadosi SC, Bhat S, Gould TD. The tail suspension test. *J Vis Exp*. 2012(59):e3769. doi: [10.3791/3769](https://doi.org/10.3791/3769)
 37. Yankelevitch-Yahav R, Franko M, Huly A, Doron R. The forced swim test as a model of depressive-like behavior. *J Vis Exp*. 2015(97):52587. doi: [10.3791/52587](https://doi.org/10.3791/52587)
 38. Pignataro P, Dicarlo M, Zerlotin R, *et al*. Antidepressant effect of intermittent long-term systemic administration of irisin in mice. *Int J Mol Sci*. 2022;23(14):7596. doi: [10.3390/ijms23147596](https://doi.org/10.3390/ijms23147596)
 40. Tiller JW. Depression and anxiety. *Med J Aust*. 2013;199(S6):S28-31. doi: [10.5694/mja12.10628](https://doi.org/10.5694/mja12.10628)
 41. Islam MR, Valaris S, Young MF, *et al*. Exercise hormone irisin is a critical regulator of cognitive function. *Nat Metab*. 2021;3(8):1058-1070. doi: [10.1038/s42255-021-00438-z](https://doi.org/10.1038/s42255-021-00438-z)
 42. Wrann CD, White JP, Salogiannis J, *et al*. Exercise induces hippocampal BDNF through a PGC-1 α /FNDC5 pathway. *Cell Metab*. 2013;18(5):649-659. doi: [10.1016/j.cmet.2013.09.008](https://doi.org/10.1016/j.cmet.2013.09.008)
 43. Wang S, Pan J. Irisin ameliorates depressive-like behaviors in rats by regulating energy metabolism. *Biochem Biophys Res Commun*. 2016;474(1):22-28. doi: [10.1016/j.bbrc.2016.04.047](https://doi.org/10.1016/j.bbrc.2016.04.047)
 44. Siteneski A, Cunha MP, Lieberknecht V, *et al*. Central irisin administration affords antidepressant-like effect and modulates neuroplasticity-related genes in the hippocampus and prefrontal cortex of mice. *Prog Neuropsychopharmacol Biol Psychiatry*. 2018;84:294-303. doi: [10.1016/j.pnpbp.2018.03.004](https://doi.org/10.1016/j.pnpbp.2018.03.004)
 44. Qi X, Wang J. Melatonin improves mitochondrial biogenesis through the AMPK/PGC1 α pathway to attenuate ischemia/reperfusion-induced myocardial damage. *Aging (Albany NY)*. 2020;12(8):7299-7312. doi: [10.18632/aging.103078](https://doi.org/10.18632/aging.103078)

45. Hardeland R, Cardinali DP, Srinivasan V, Spence DW, Brown GM, Pandi-Perumal SR. Melatonin--a pleiotropic, orchestrating regulator molecule. *Prog Neurobiol.* 2011;93(3):350-384. doi: [10.1016/j.pneurobio.2010.12.004](https://doi.org/10.1016/j.pneurobio.2010.12.004)
46. Reiter RJ, Mayo JC, Tan DX, Sainz RM, Alatorre-Jimenez M, Qin L. Melatonin as an antioxidant: Under promises but over delivers. *J Pineal Res.* 2016;61(3):253-278. doi: [10.1111/jpi.12360](https://doi.org/10.1111/jpi.12360)
47. Gul-Kahraman K, Yilmaz-Bozoglan M, Sahna E. Physiological and pharmacological effects of melatonin on remote ischemic preconditioning after myocardial ischemia-reperfusion injury in rats: Role of Cybb, Fas, NfκappaB, Irisin signaling pathway. *J Pineal Res.* 2019;67(2):e12589. doi: [10.1111/jpi.12589](https://doi.org/10.1111/jpi.12589)
48. Ouyang H, Li Q, Zhong J, et al. Combination of melatonin and irisin ameliorates lipopolysaccharide-induced cardiac dysfunction through suppressing the Mst1-JNK pathways. *J Cell Physiol.* 2020;235(10):6647-6659. doi: [10.1002/jcp.29561](https://doi.org/10.1002/jcp.29561)
49. Tobeiha M, Jafari A, Fadaei S, et al. Evidence for the benefits of melatonin in cardiovascular disease. *Front Cardiovasc Med.* 2022;9:888319. doi: [10.3389/fcvm.2022.888319](https://doi.org/10.3389/fcvm.2022.888319)
50. Gabriel BM, Zierath JR. Circadian rhythms and exercise - re-setting the clock in metabolic disease. *Nat Rev Endocrinol.* 2019;15(4):197-206. doi: [10.1038/s41574-018-0150-x](https://doi.org/10.1038/s41574-018-0150-x)
51. Guo M, Shen F, Guo X, et al. BMAL1/PGC1α/IRIN axis impacts distinct outcomes of time-of-day resistance exercise. *J Sport Health Sci.* 2024;14:100968. doi: [10.1016/j.jshs.2024.100968](https://doi.org/10.1016/j.jshs.2024.100968)
52. Hiragaki S, Baba K, Coulson E, Kunst S, Spessert R, Tosini G. Melatonin signaling modulates clock genes expression in the mouse retina. *PLoS One.* 2014;9(9):e106819. doi: [10.1371/journal.pone.0106819](https://doi.org/10.1371/journal.pone.0106819)
53. Dong B, Xie C, Jing X, Lin L, Tian L. Yoga has a solid effect on cancer-related fatigue in patients with breast cancer: A meta-analysis. *Breast Cancer Res Treat.* 2019;177(1):5-16. doi: [10.1007/s10549-019-05278-w](https://doi.org/10.1007/s10549-019-05278-w)
54. Kishan P. Yoga and spirituality in mental health: Illness to wellness. *Indian J Psychol Med.* 2020;42(5):411-420. doi: [10.1177/0253717620946995](https://doi.org/10.1177/0253717620946995)
55. Bower JE, Garet D, Sternlieb B, et al. Yoga for persistent fatigue in breast cancer survivors: A randomized controlled trial. *Cancer.* 2012;118(15):3766-3775. doi: [10.1002/cncr.26702](https://doi.org/10.1002/cncr.26702)
56. Banasik J, Williams H, Haberman M, Blank SE, Bendel R. Effect of Iyengar yoga practice on fatigue and diurnal salivary cortisol concentration in breast cancer survivors. *J Am Acad Nurse Pract.* 2011;23(3):135-142. doi: [10.1111/j.1745-7599.2010.00573.x](https://doi.org/10.1111/j.1745-7599.2010.00573.x)
57. Banerjee B, Vadiraj HS, Ram A, et al. Effects of an integrated yoga program in modulating psychological stress and radiation-induced genotoxic stress in breast cancer patients undergoing radiotherapy. *Integr Cancer Ther.* 2007;6(3):242-250. doi: [10.1177/1534735407306214](https://doi.org/10.1177/1534735407306214)
58. Mustian KM. Yoga as treatment for insomnia among cancer patients and survivors: A systematic review. *Eur Med J Oncol.* 2013;1:106-115.
59. Zhu J, Chen X, Zhen X, et al. Meta-analysis of effects of yoga exercise intervention on sleep quality in breast cancer patients. *Front Oncol.* 2023;13:1146433. doi: [10.3389/fonc.2023.1146433](https://doi.org/10.3389/fonc.2023.1146433)
60. Carson JW, Carson KM, Porter LS, Keefe FJ, Seewaldt VL. Yoga of Awareness program for menopausal symptoms in breast cancer survivors: Results from a randomized trial. *Support Care Cancer.* 2009;17(10):1301-1309. doi: [10.1007/s00520-009-0587-5](https://doi.org/10.1007/s00520-009-0587-5)
61. Yagli NV, Ulger O. The effects of yoga on the quality of life and depression in elderly breast cancer patients. *Complement Ther Clin Pract.* 2015;21(1):7-10. doi: [10.1016/j.ctcp.2015.01.002](https://doi.org/10.1016/j.ctcp.2015.01.002)
62. Rao RM, Vadiraja HS, Nagaratna R, et al. Effect of yoga on sleep quality and neuroendocrine immune response in metastatic breast cancer patients. *Indian J Palliat Care.* 2017;23(3):253-260. doi: [10.4103/IJPC.IJPC_102_17](https://doi.org/10.4103/IJPC.IJPC_102_17)
63. Wang WL, Chen KH, Pan YC, Yang SN, Chan YY. The effect of yoga on sleep quality and insomnia in women with sleep problems: A systematic review and meta-analysis. *BMC Psychiatry.* 2020;20(1):195. doi: [10.1186/s12888-020-02566-4](https://doi.org/10.1186/s12888-020-02566-4)
64. Sadokpam B, Bera TK. Effect of yoga exercises on irisin hormone in obese people. *Int J Health Sci Res.* 2018;8(6):158-163.
65. Budhrani-Shani P, Berry DL, Arcari P, Langevin H, Wayne PM. Mind-body exercises for nurses with chronic low back pain: An evidence-based review. *Nurs Res Pract.* 2016;2016:9018036. doi: [10.1155/2016/9018036](https://doi.org/10.1155/2016/9018036)
66. Han D, Cheng J, Qu J, et al. Effectiveness of Taijiquan in treating insomnia: A systematic review and meta-analysis of randomized controlled studies. *Front Psychiatry.* 2022;13:892453. doi: [10.3389/fpsy.2022.892453](https://doi.org/10.3389/fpsy.2022.892453)

67. Li H, Chen J, Xu G, *et al.* The effect of Tai Chi for improving sleep quality: A systematic review and meta-analysis. *J Affect Disord.* 2020;274:1102-1112. doi: [10.1016/j.jad.2020.05.076](https://doi.org/10.1016/j.jad.2020.05.076)
68. Yang Z, Zhai H, Yang Z, Ning B. Comparing the efficacy of traditional Chinese exercises and general aerobic exercises in university students with sleep disorders: A systematic review and meta-analysis. *Medicine (Baltimore).* 2024;103(23):e38521. doi: [10.1097/MD.00000000000038521](https://doi.org/10.1097/MD.00000000000038521)
69. Vanderlinden J, Boen F, van Uffelen JGZ. Effects of physical activity programs on sleep outcomes in older adults: A systematic review. *Int J Behav Nutr Phys Act.* 2020;17(1):11. doi: [10.1186/s12966-020-0913-3](https://doi.org/10.1186/s12966-020-0913-3)
70. Guazzarini AG, Mancinetti F, Bastiani P, *et al.* Tai chi, irisin and cognitive performance: A clinical and biological investigation in older adults. *Aging Clin Exp Res.* 2024;36(1):90. doi: [10.1007/s40520-024-02743-5](https://doi.org/10.1007/s40520-024-02743-5)
71. Lyu L, Li Y, Fan X, Seo J, Eunna O. The effect of Tai Chi exercise intervention on sleep quality in community residing older adults: A systematic review and meta-analysis. *Eur Geriatr Med.* 2024;15(2):381-396. doi: [10.1007/s41999-023-00923-6](https://doi.org/10.1007/s41999-023-00923-6)
72. Whitworth JW, Nosrat S, SantaBarbara NJ, Ciccolo JT. Feasibility of resistance exercise for posttraumatic stress and anxiety symptoms: A randomized controlled pilot study. *J Trauma Stress.* 2019;32(6):977-984. doi: [10.1002/jts.22464](https://doi.org/10.1002/jts.22464)
73. Syed-Abdul MM. Benefits of resistance training in older adults. *Curr Aging Sci.* 2021;14(1):5-9. doi: [10.2174/1874609813999201110192221](https://doi.org/10.2174/1874609813999201110192221)
74. Langlais CS, Chen YH, Van Blarigan EL, *et al.* Quality of life for men with metastatic castrate-resistant prostate cancer participating in an aerobic and resistance exercise pilot intervention. *Urol Oncol.* 2023;41(3):146.e1-e111. doi: [10.1016/j.urolonc.2022.11.016](https://doi.org/10.1016/j.urolonc.2022.11.016)
75. Piraux E, Reyckler G, Vancraeynest D, Geets X, Leonard D, Caty G. High-intensity aerobic interval training and resistance training are feasible in rectal cancer patients undergoing chemoradiotherapy: A feasibility randomized controlled study. *Rep Pract Oncol Radiother.* 2022;27(2):198-208. doi: [10.5603/RPOR.a2022.0036](https://doi.org/10.5603/RPOR.a2022.0036)
76. Piraux E, Caty G, Renard L, *et al.* Effects of high-intensity interval training compared with resistance training in prostate cancer patients undergoing radiotherapy: A randomized controlled trial. *Prostate Cancer Prostatic Dis.* 2021;24(1):156-165. doi: [10.1038/s41391-020-0259-6](https://doi.org/10.1038/s41391-020-0259-6)
77. Maric D, Ficarra S, Di Bartolo L, *et al.* Effects of resistance training on sleep quality and disorders among individuals diagnosed with cancer: A systematic review and meta-analysis of randomized controlled trials. *Cancer Med.* 2024;13(8):e7179. doi: [10.1002/cam4.7179](https://doi.org/10.1002/cam4.7179)
78. Kovacevic A, Mavros Y, Heisz JJ, Fiatarone Singh MA. The effect of resistance exercise on sleep: A systematic review of randomized controlled trials. *Sleep Med Rev.* 2018;39:52-68. doi: [10.1016/j.smrv.2017.07.002](https://doi.org/10.1016/j.smrv.2017.07.002)
79. Monico-Neto M, Antunes HK, Lee KS, *et al.* Resistance training minimizes catabolic effects induced by sleep deprivation in rats. *Appl Physiol Nutr Metab.* 2015;40(11):1143-1150. doi: [10.1139/apnm-2015-0061](https://doi.org/10.1139/apnm-2015-0061)
80. Kim HJ, So B, Choi M, Kang D, Song W. Resistance exercise training increases the expression of irisin concomitant with improvement of muscle function in aging mice and humans. *Exp Gerontol.* 2015;70:11-17. doi: [10.1016/j.exger.2015.07.006](https://doi.org/10.1016/j.exger.2015.07.006)
81. Cosio PL, Crespo-Posadas M, Velarde-Sotres A, Pelaez M. Effect of chronic resistance training on circulating irisin: Systematic review and meta-analysis of randomized controlled trials. *Int J Environ Res Public Health.* 2021;18(5):2476. doi: [10.3390/ijerph18052476](https://doi.org/10.3390/ijerph18052476)
82. Faraguna U, Vyazovskiy VV, Nelson AB, Tononi G, Cirelli C. A causal role for brain-derived neurotrophic factor in the homeostatic regulation of sleep. *J Neurosci.* 2008;28(15):4088-4095. doi: [10.1523/JNEUROSCI.5510-07.2008](https://doi.org/10.1523/JNEUROSCI.5510-07.2008)
83. Frimpong E, Mograss M, Zvionow T, Dang-Vu TT. The effects of evening high-intensity exercise on sleep in healthy adults: A systematic review and meta-analysis. *Sleep Med Rev.* 2021;60:101535. doi: [10.1016/j.smrv.2021.101535](https://doi.org/10.1016/j.smrv.2021.101535)
84. Weinert D, Gubin D. The impact of physical activity on the circadian system: Benefits for health, performance and wellbeing. *Appl Sci.* 2022;12(18):9220.
85. Edwards B, Waterhouse J, Atkinson G, Reilly T. Exercise does not necessarily influence the phase of the circadian rhythm in temperature in healthy humans. *J Sports Sci.* 2002;20(9):725-732. doi: [10.1080/026404102320219437](https://doi.org/10.1080/026404102320219437)
86. Youngstedt SD, Elliott JA, Kripke DF. Human circadian phase-response curves for exercise. *J Physiol.* 2019;597(8):2253-2268. doi: [10.1113/jp276943](https://doi.org/10.1113/jp276943)
87. Buxton OM, Lee CW, L'Hermite-Baleriaux M,

Turek FW, Van Cauter E. Exercise elicits phase shifts and acute alterations of melatonin that vary with circadian phase. *Am J Physiol Regul Integr Comp Physiol.* 2003;284(3):R714-R724. doi: 10.1152/ajpregu.00355.2002

88. Yamanaka Y, Hashimoto S, Takasu NN, *et al.* Morning and evening physical exercise differentially regulate the autonomic nervous system during nocturnal sleep in humans. *Am J Physiol Regul Integr Comp Physiol.* 2015;309(9):R1112-R1121. doi: 10.1152/ajpregu.00127.2015

89. Hunter GR, Brock DW, Byrne NM, Chandler-Laney PC, Del Corral P, Gower BA. Exercise training prevents regain of visceral fat for 1 year following weight loss. *Obesity (Silver Spring).* 2010;18(4):690-695. doi: 10.1038/oby.2009.316

90. Rubio-Sastre P, Gomez-Abellan P, Martinez-Nicolas A, Ordovas JM, Madrid JA, Garaulet M. Evening physical activity alters wrist temperature circadian rhythmicity. *Chronobiol Int.* 2014;31(2):276-282. doi: 10.3109/07420528.2013.833215

91. Anastasilakis AD, Polyzos SA, Saridakis ZG, *et al.* Circulating irisin in healthy, young individuals: Day-night rhythm, effects of food intake and exercise, and associations with gender, physical activity, diet, and body composition. *J Clin Endocrinol Metab.* 2014;99(9):3247-3255. doi: 10.1210/jc.2014-1367

92. Takemura N, Cheung DST, Smith R, *et al.* Effectiveness of aerobic exercise and mind-body exercise in cancer patients with poor sleep quality: A systematic review and meta-analysis of randomized controlled trials. *Sleep Med Rev.* 2020;53:101334. doi: 10.1016/j.smrv.2020.101334

93. Aton SJ, Herzog ED. Come together, right. now: Synchronization of rhythms in a mammalian circadian clock. *Neuron.* 2005;48(4):531-534. doi: 10.1016/j.neuron.2005.11.001

94. Liu C, Li S, Liu T, Borjigin J, Lin JD. Transcriptional coactivator PGC-1 α integrates the mammalian clock and energy metabolism. *Nature.* 2007;447(7143):477-481. doi: 10.1038/nature05767

95. Ferrell JM, Chiang JY. Circadian rhythms in liver metabolism and disease. *Acta Pharm Sin B.* 2015;5(2):113-122. doi: 10.1016/j.apsb.2015.01.003

96. Khan S, Nobili L, Khatami R, *et al.* Circadian rhythm and epilepsy. *Lancet Neurol.* 2018;17(12):1098-1108. doi: 10.1016/S1474-4422(18)30335-1

97. Boström P, Wu J, Jedrychowski MP, *et al.* A PGC1- α -dependent myokine that drives brown-fat-like development of white fat and thermogenesis. *Nature.* 2012;481(7382):463-468. doi: 10.1038/

nature10777

98. Ruas JL, White JP, Rao RR, *et al.* A PGC-1 α isoform induced by resistance training regulates skeletal muscle hypertrophy. *Cell.* 2012;151(6):1319-1331. doi: 10.1016/j.cell.2012.10.050

99. Martinez-Redondo V, Pettersson AT, Ruas JL. The hitchhiker's guide to PGC-1 α isoform structure and biological functions. *Diabetologia.* 2015;58(9):1969-1977. doi: 10.1007/s00125-015-3671-z

100. Puigserver P, Wu Z, Park CW, Graves R, Wright M, Spiegelman BM. A cold-inducible coactivator of nuclear receptors linked to adaptive thermogenesis. *Cell.* 1998;92(6):829-839. doi: 10.1016/S0092-8674(00)81410-5

101. Ryan MT, Hoogenraad NJ. Mitochondrial-nuclear communications. *Annu Rev Biochem.* 2007;76:701-722. doi: 10.1146/annurev.biochem.76.052305.091720

102. Masri S, Sassone-Corsi P. The emerging link between cancer, metabolism, and circadian rhythms. *Nat Med.* 2018;24(12):1795-1803. doi: 10.1038/s41591-018-0271-8

103. Sedliak M, Zeman M, Buzgo G, *et al.* Morphological, molecular and hormonal adaptations to early morning versus afternoon resistance training. *Chronobiol Int.* 2018;35(4):450-464. doi: 10.1080/07420528.2017.1411360

104. Savikj M, Gabriel BM, Alm PS, *et al.* Afternoon exercise is more efficacious than morning exercise at improving blood glucose levels in individuals with type 2 diabetes: A randomised crossover trial. *Diabetologia.* 2019;62(2):233-237. doi: 10.1007/s00125-018-4767-z

105. Zhang B, Wing YK. Sex differences in insomnia: A meta-analysis. *Sleep.* 2006;29(1):85-93. doi: 10.1093/sleep/29.1.85

106. Kische H, Ewert R, Fietze I, *et al.* Sex Hormones and sleep in men and women from the general population: A cross-sectional observational study. *J Clin Endocrinol Metab.* 2016;101(11):3968-3977. doi: 10.1210/jc.2016-1832

107. Calhoun SL, Fernandez-Mendoza J, Vgontzas AN, Liao D, Bixler EO. Prevalence of insomnia symptoms in a general population sample of young children and preadolescents: gender effects. *Sleep Med.* 2014;15(1):91-95. doi: 10.1016/j.sleep.2013.08.787

108. Kizilirmak A, Timur S, Kartal B. Insomnia

in pregnancy and factors related to insomnia. *ScientificWorldJournal*. 2012;2012:197093. doi: 10.1100/2012/197093

109. PengoMF, WonCH, BourjeilyG. Sleep in women across the life span. *Chest*. 2018;154(1):196-206. doi: 10.1016/j.chest.2018.04.005

110. Dorsey A, de Lecea L, Jennings KJ. Neurobiological and hormonal mechanisms regulating women's sleep. *Front Neurosci*. 2020;14:625397. doi: 10.3389/fnins.2020.625397

111. Andersen ML, Hachul H, Ishikura IA, Tufik S. Sleep in women: A narrative review of hormonal influences, sex differences and health implications. *Front Sleep*. 2023;2:1271827. doi: 10.3389/frsle.2023.1271827

112. Rubio-Arias JA, Marin-Cascales E, Ramos-Campo DJ, Hernandez AV, Perez-Lopez FR. Effect of exercise on sleep quality and insomnia in middle-aged women: A systematic review and meta-analysis of randomized controlled trials. *Maturitas*. 2017;100:49-56. doi: 10.1016/j.maturitas.2017.04.003

113. Yang SY, Lan SJ, Yen YY, Hsieh YP, Kung PT, Lan SH. Effects of exercise on sleep quality in pregnant women: A systematic review and meta-analysis of randomized controlled trials. *Asian Nurs Res (Korean Soc Nurs Sci)*. 2020;14(1):1-10.

doi: 10.1016/j.anr.2020.01.003

114. Luo Y, Qiao X, Xu L, Huang G. Irisin: Circulating levels in serum and its relation to gonadal axis. *Endocrine*. 2022;75(3):663-671. doi: 10.1007/s12020-022-02981-5

115. Hadjimarkou MM, Benham R, Schwarz JM, Holder MK, Mong JA. Estradiol suppresses rapid eye movement sleep and activation of sleep-active neurons in the ventrolateral preoptic area. *Eur J Neurosci*. 2008;27(7):1780-1792. doi: 10.1111/j.1460-9568.2008.06142.x

116. Beekly B, Furman K, Burgess C, Elias C. KNDy innervation of MCH neurons modulates sleep in an estradiol-dependent manner. *Physiology*. 2023;38:5732862. doi: 10.1152/physiol.2023.38.S1.5732862

117. Furukawa TA, Noma H, Caldwell DM, et al. Waiting list may be a placebo condition in psychotherapy trials: A contribution from network meta-analysis. *Acta Psychiatr Scand*. 2014;130(3):181-192. doi: 10.1111/acps.12275

118. Xie Y, Liu S, Chen XJ, Yu HH, Yang Y, Wang W. Effects of exercise on sleep quality and insomnia in adults: A systematic review and meta-analysis of randomized controlled trials. *Front Psychiatry*. 2021;12:664499. doi: 10.3389/fpsy.2021.664499