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REVIEW

Insomnia Pathogenesis and Multidimensional Mechanisms of Acupuncture: A Narrative Review

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Objective: Insomnia is a common sleep disorder marked by difficulties in sleep initiation, maintenance, and daytime performance. Pharmacological treatments offer short-term relief but are limited by tolerance, dependence, and adverse effects. This review aims to evaluate recent advances in acupuncture for insomnia, with emphasis on clinical efficacy and underlying mechanisms.

Methods: This narrative review was conducted through a structured literature search of PubMed, Web of Science, and CNKI databases covering studies published from January 2020 to December 2025. The search combined keywords including "insomnia", "acupuncture", "mechanism", "autonomic nervous system", "inflammation", and "HPA axis". Both clinical and preclinical studies published in English or Chinese were considered. Studies were screened based on relevance to acupuncture interventions for insomnia and mechanistic outcomes. Although a formal systematic review protocol was not applied, emphasis was placed on representative and high-quality evidence to summarize key mechanistic pathways.

Results: Evidence suggests that acupuncture improves subjective sleep quality, alleviates hyperarousal, reduces systemic inflammation, and promotes neuroimmune balance through multidimensional mechanisms. However, limitations remain, including small sample sizes, methodological heterogeneity, inadequate blinding, and insufficient mechanistic exploration.

Conclusion: Acupuncture is a promising integrative intervention for insomnia with both symptomatic and mechanistic benefits. Future studies should prioritize large-scale, multicenter randomized controlled trials and standardized protocols, while incorporating multi-omics, neuroimaging, and precision medicine approaches. Interdisciplinary collaboration may advance acupuncture from empirical therapy to precision medicine, providing new opportunities for comprehensive insomnia management.

Keywords: acupuncture, insomnia, autonomic nervous system, inflammation, HPA axis, precision medicine

Introduction

Insomnia is a prevalent sleep disorder characterized by difficulty initiating sleep, impaired sleep maintenance, or early awakening, often accompanied by daytime functional impairment.[1] In recent years, the accelerated pace of life and increased psychological stress have contributed to a rising incidence of insomnia, imposing a substantial burden on both individual quality of life and public health. The 2023 China Healthy Sleep White Paper reported that approximately 60.4% of the Chinese population experiences varying degrees of sleep disturbances.[2] Among these, insomnia is the most common subtype, with about 10% of adults experiencing persistent symptoms; notably, its prevalence is significantly higher in women than in men (17.6% vs 10.1%).[3] Evidence indicates that sleep disorders not only cause abnormalities in serological markers and immune dysfunction but are also strongly associated with severe physical and mental illnesses, including hypertension, depression, and cardiovascular disease.[4,5] Current clinical treatments primarily include cognitive behavioral therapy for insomnia (CBT-I) and pharmacological interventions.[6,7] However, CBT-I faces challenges in terms

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of specificity and adherence, while pharmacological treatments are often accompanied by side effects, tolerance, and dependency.[8,9] Therefore, there is an urgent need for safe, effective, and sustainable therapeutic strategies.

As an integral component of traditional Chinese medicine, acupuncture has gained increasing global attention and recognition. Substantial research supports its application across multiple clinical disciplines, including neurology, musculoskeletal medicine, obstetrics and gynecology, oncology, and gastroenterology.[10,11] Acupuncture, a therapy with minimal adverse effects, shows unique advantages in the treatment of insomnia and has gradually achieved international recognition.[12] Clinical studies demonstrate that acupuncture can significantly improve sleep quality and duration[13] and is superior to sham acupuncture in enhancing sleep efficiency and reducing insomnia severity.[14] Basic and translational research further suggests multiple mechanisms underlying these effects: acupuncture stimulates neuronal activity in the brain,[15] regulates the synthesis and release of sleep-related neurotransmitters such as catecholamines, glutamate, and melatonin,[16] and increases nitric oxide levels in both central and peripheral systems.[17] Moreover, accumulating evidence indicates that acupuncture modulates autonomic nervous system function,[18] and neuroimaging studies suggest that it alters functional connectivity and activity across brain regions associated with sleep regulation.[19,20] Nonetheless, despite robust evidence of its efficacy, the precise central regulatory mechanisms of acupuncture remain incompletely understood, limiting its clinical translation and broader application.

To further clarify the research landscape, we analyzed the number of publications on acupuncture and insomnia indexed in CNKI and PubMed from 2020 to 2025 (Figure 1). The results revealed that CNKI publications have increased rapidly since 2020, especially after 2025, reflecting growing domestic attention and widespread clinical application of acupuncture in insomnia treatment. In contrast, PubMed publications, although fewer in number, have shown a steady increase since the early 2000s, with greater emphasis on randomized controlled trials and mechanistic investigations. This discrepancy highlights differences in research priorities: domestic studies focus mainly on clinical efficacy and practical applications, while international studies emphasize evidence-based validation and mechanistic exploration. These findings suggest that future research should integrate the strengths of both domestic and international perspectives to promote standardization, internationalization, and mechanistic elucidation of acupuncture for insomnia. Despite increasing evidence supporting acupuncture for insomnia, several critical gaps remain. First, the underlying mechanisms of acupuncture are still debated, with inconsistencies reported in neuroimaging findings and biomarker studies, partly due to heterogeneity in study design and stimulation protocols. Second, although cognitive behavioral therapy for insomnia (CBT-I) is recommended as first-line treatment, its long-term adherence and accessibility remain limited, whereas acupuncture may offer a complementary or alternative approach with distinct advantages in certain patient populations. Accordingly, this narrative review was based on literature retrieved from PubMed, Web of Science, and CNKI databases. Relevant studies published in English and Chinese were screened, focusing on clinical efficacy and mechanistic insights of acupuncture in insomnia, including neuroendocrine regulation, autonomic function, and inflammatory pathways. Importantly, this review focuses on three core mechanistic

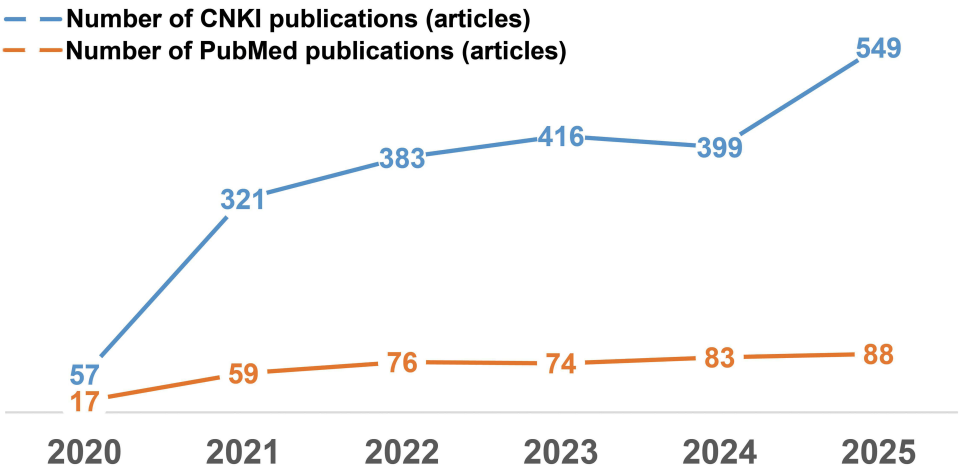

Figure 1 Publication trends on acupuncture and insomnia in CNKI and PubMed (2020–2025).

domains—autonomic nervous system (ANS) regulation, inflammatory modulation, and hypothalamic–pituitary–adrenal (HPA) axis activity—because they are central to the hyperarousal model of insomnia. However, other emerging mechanisms, including circadian clock gene regulation and the gut–brain axis, may also contribute to acupuncture effects and warrant further investigation. By defining this scope, we aim to provide a focused yet integrative synthesis of current evidence while highlighting directions for future research.

Pathophysiology of Insomnia

Neurotransmitter Imbalance

Neurotransmitters such as γ-aminobutyric acid (GABA), serotonin (5-HT), melatonin (MT), and cortisol are essential mediators of neuronal communication, playing key roles in emotional regulation, cognitive function, and maintenance of the sleep–wake cycle.[21] Neurotransmitter imbalance—defined as abnormal concentrations or activities that impair neural transmission—can trigger a wide range of physiological and psychological disturbances, including insomnia.[22,23]

GABA

GABA is a non-proteinogenic amino acid synthesized from L-glutamate through glutamate decarboxylase–mediated decarboxylation.[24] As the principal inhibitory neurotransmitter in the mammalian central nervous system, GABA is widely distributed throughout the brain, with particularly high concentrations in the hippocampus, hypothalamus, basal ganglia, and cerebral cortex.[25] During rest, abundant GABA release enhances inhibitory signaling, thereby promoting relaxation, reducing anxiety, and maintaining network stability.[26,27] Approximately one-third of central nervous system synapses rely on GABAergic transmission, underscoring its fundamental role in regulating neural activity.[28]

The sleep-promoting effect of GABA depends primarily on its binding to ligand-gated Cl^- channels. Activation of GABA_A receptors triggers Cl^- influx, leading to neuronal hyperpolarization and suppression of action potential firing, which prevents hyperexcitability and produces sedative and hypnotic effects (Figure 2A).[29] In addition, GABA_B receptors, which are G protein–coupled, mediate slower and prolonged inhibitory signaling by activating inwardly rectifying K^+ currents and inhibiting Ca^{2+} influx, further contributing to sleep maintenance. GABA_C receptors, though more restricted in distribution, provide specialized inhibitory regulation, particularly in the visual system. Together, these receptor subtypes orchestrate different aspects of inhibitory tone relevant to sleep–wake regulation.

Clinical and experimental studies consistently highlight GABA's critical role in sleep physiology. For instance, Xiang et al[30] reported significantly reduced brain GABA levels in insomnia patients compared with normal sleepers, with

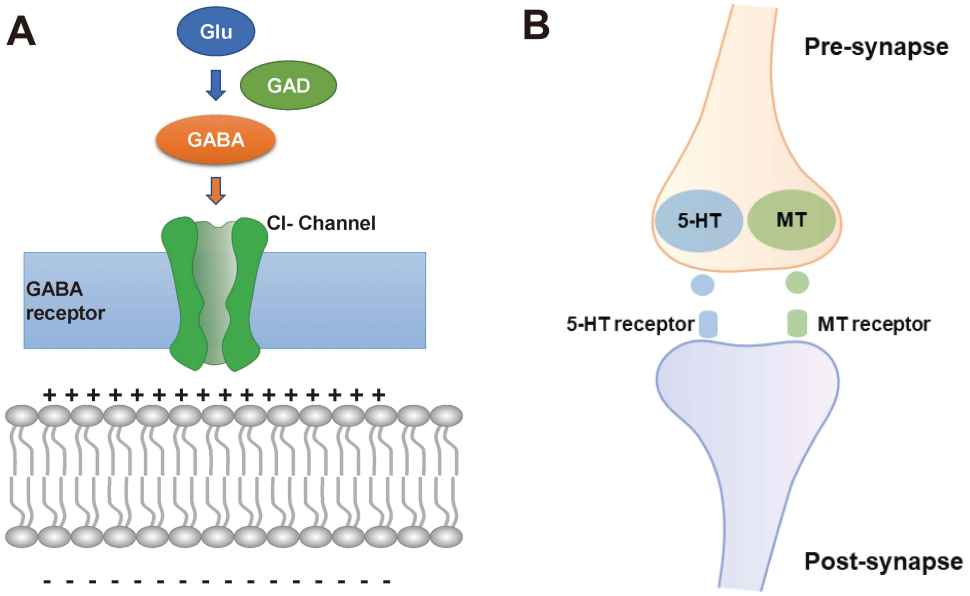

Figure 2 GABA, 5-HT and MT improve the sleep mechanism. (**A**) GABA. (**B**) 5-HT and MT.

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reductions positively correlated with insomnia severity. Similarly, magnetic resonance spectroscopy (MRS) studies have confirmed diminished GABA concentrations in the anterior cingulate cortex and occipital regions of insomnia patients, supporting the hypothesis of impaired inhibitory control in hyperarousal states. Other studies have shown that mRNA expression of GABA_A receptor α1 and α2 subunits is markedly downregulated in insomnia patients, whereas peripheral serum GABA concentrations show no significant difference between insomnia and controls.[31] These findings suggest that, beyond absolute GABA levels, alterations in receptor subunit composition and regional GABAergic tone may serve as important molecular markers of sleep quality.

Furthermore, pharmacological evidence reinforces the essential role of GABA in sleep regulation. Many widely prescribed hypnotics, including benzodiazepines and non-benzodiazepine "Z-drugs", exert their therapeutic effect by enhancing GABA_A receptor activity, particularly through the α1 subunit, which mediates sedative and hypnotic effects.[32] Novel agents such as gabapentin and pregabalin indirectly augment GABAergic transmission and have shown efficacy in improving sleep continuity in clinical settings. Animal studies also demonstrate that genetic knockout or pharmacological blockade of GABA_A receptor subunits disrupts normal sleep architecture, leading to reduced non-rapid eye movement (NREM) sleep and fragmented sleep cycles.[33]

Taken together, converging lines of evidence from neurochemical, molecular, imaging, and pharmacological studies indicate that GABAergic dysfunction constitutes a central mechanism in the pathogenesis of insomnia. Both diminished GABA availability and receptor subunit dysregulation impair inhibitory control, thereby sustaining hyperarousal and preventing normal sleep initiation and maintenance.

Serotonin (5-HT) and Melatonin (MT)

5-HT, an indole derivative, is widely distributed in the central nervous system, gastrointestinal tract, and platelets, and acts as a key neurotransmitter in sleep regulation.[34] In the brain, serotonergic neurons arise primarily from the raphe nuclei and project extensively to the forebrain, hippocampus, thalamus, and hypothalamus, regions critically involved in arousal and sleep–wake regulation. Beyond its central functions, peripheral 5-HT also influences gut motility and immune signaling, both of which have indirect effects on circadian physiology.[35] Melatonin (MT), secreted by the pineal gland, is synthesized from 5-HT through sequential acetylation and methylation.[36] MT primarily alleviates sleep disturbances caused by circadian rhythm disruption by resetting biological rhythms.[37]

Among the various 5-HT receptor subtypes, the 5-HT1A receptor is most strongly implicated in sleep regulation. It is localized to serotonergic neuronal synapses, glutamatergic neurons of the frontal/parietal cortex and hippocampus, and dopaminergic, noradrenergic, and cholinergic neurons in the striatum and midbrain.[38] Activation of the 5-HT1A receptor suppresses serotonin release, inhibits glutamatergic pyramidal neuron activity, and enhances the release of dopamine, norepinephrine, and acetylcholine. As a G protein–coupled receptor, 5-HT1A regulates adenylate cyclase via Gαi/o subunits, modulating cyclic adenosine monophosphate (cAMP) signaling and thereby influencing emotional and arousal states.[39] Notably, the dual role of 5-HT in promoting both wakefulness and sleep depends on receptor subtype, regional distribution, and circadian timing.

Experimental studies confirm the role of serotonergic signaling in sleep. Qian et al[40] demonstrated that deletion of tryptophan hydroxylase (Trh) or certain 5-HT receptor subtypes (5-HT1A, 5-HT2B) shortened sleep duration, while loss of Trh or 5-HT2B attenuated rebound sleep after deprivation, indicating the critical role of serotonergic pathways. Dugovic further found that 5-HT inhibits slow-wave sleep (SWS) through 5-HT2 receptors, whose activity exhibits circadian variation, likely linked to MT-mediated circadian rhythms.[41] Complementary findings suggest that 5-HT2C receptor activation contributes to sleep fragmentation and reduced NREM sleep stability, while blockade of 5-HT2A/2C receptors improves sleep continuity.[42]

The sleep-promoting effects of MT are closely associated with regulation of hypothalamic GABA synthase. Three MT receptor subtypes—MT1, MT2, and MT3—have been identified in mammals. MT binding to MT1/MT2 receptors activates hypothalamic GABA synthase, increasing GABA levels and synergistically reducing sleep latency while prolonging sleep duration. Gobbi and Comai reported that MT1 receptors mainly regulate rapid eye movement (REM) sleep, whereas MT2 receptors preferentially promote non-REM (NREM) sleep, with distinct brain distributions.[43] Although MT functions through G protein–coupled receptors, its downstream molecular targets remain incompletely defined.

Recent evidence has identified additional targets. Niu et al[44] showed in Caenorhabditis elegans that the BK channel slo-1 is a direct molecular target of the MT receptor pcdr-1. Knockout of pcdr-1, slo-1, or the MT synthesis–related gene homt-1 increased excitatory neurotransmitter release and shortened sleep duration. These findings suggest that MT promotes sleep by activating BK channels through specific receptors and associated G protein subunits (Gβλ) (Figure 2B). In addition, mammalian studies indicate that MT influences clock gene expression (eg, Per1, Cry1), thereby aligning circadian pacemaker activity with the external light–dark cycle.[45] Clinical trials further demonstrate that exogenous MT supplementation improves sleep onset latency and circadian rhythm disorders such as delayed sleep–wake phase syndrome and jet lag, highlighting its therapeutic value.[46]

Collectively, the serotonergic–melatonergic pathway exerts multi-level regulation of sleep. While 5-HT directly modulates neuronal excitability via its receptor subtypes, MT fine-tunes circadian rhythmicity and GABAergic signaling to optimize sleep quality. Disruptions in either neurotransmitter or receptor function may therefore serve as critical neurochemical signatures of insomnia and other sleep disorders.

Cortisol

Cortisol, a hormone central to the stress response, exhibits pronounced circadian fluctuations in secretion, with peak levels occurring in the early morning and a gradual decline throughout the day.[47] This diurnal rhythm is critical for maintaining energy balance, immune function, and cognitive performance. Disruption of this rhythm, particularly elevated nocturnal cortisol and a flattened diurnal slope, has been closely linked to impaired sleep initiation and maintenance. Within the framework of the hyperarousal hypothesis, insomnia is characterized not simply by increased cortisol levels, but by temporal dysregulation of HPA axis activity, especially excessive activation during the biological night. Importantly, cortisol should not be regarded as uniformly pathological; rather, its physiological effects are highly dependent on circadian timing. Elevated nighttime cortisol contributes to heightened arousal and sleep fragmentation, whereas appropriate daytime cortisol levels are essential for normal metabolic and cognitive function. Therefore, it is the loss of circadian specificity, rather than absolute cortisol elevation alone, that underlies its pathological role in insomnia.[48]

This observation supports the hyperarousal hypothesis of insomnia, in which elevated cortisol levels activate the hypothalamic–pituitary–adrenal (HPA) axis stress response.[49] Roehrs and Roth[50] further demonstrated that cortisol levels measured in urine and saliva during the day and at bedtime were closely linked to insomnia severity. Compared with controls, patients with insomnia showed significantly higher bedtime salivary cortisol, suggesting excessive arousal before sleep. Moreover, patients with heightened daytime alertness, particularly during multiple sleep latency tests, had significantly elevated urinary cortisol compared with healthy individuals.

Additional studies provide evidence that insomnia is associated not only with increased cortisol levels but also with altered circadian regulation of the HPA axis.[51] For example, insomnia patients often display a flattened diurnal cortisol slope, with persistently high evening cortisol that counteracts normal sleep drive. Neuroimaging studies further suggest that hyperactivation of the amygdala and prefrontal cortex during stress responses may sustain HPA axis activation, reinforcing the cycle of hyperarousal and sleep disturbance.[52] Importantly, elevated cortisol disrupts inhibitory neurotransmission by reducing GABAergic activity and interfering with melatonin synthesis, thereby linking stress hormone dysregulation with other neurochemical pathways involved in sleep regulation.[53]

From a clinical perspective, chronic activation of the HPA axis in insomnia has significant implications. Persistent hypercortisolemia has been associated with increased risks of anxiety, depression, cardiovascular disease, metabolic syndrome, and impaired immune function.[54] Longitudinal studies suggest that insomnia with concurrent cortisol dysregulation is a predictor of major depressive disorder onset, underscoring the relevance of HPA axis biomarkers in identifying individuals at high risk.[55] Interventions such as cognitive-behavioral therapy for insomnia (CBT-I) and mindfulness-based stress reduction have been shown to normalize cortisol rhythms, highlighting the therapeutic potential of targeting stress physiology to improve sleep outcomes.[56]

Central Nervous System Abnormalities

Dysfunction of the autonomic nervous system (ANS) is regarded as one of the core mechanisms in the pathophysiology of insomnia.[57] It is typically characterized by excessive sympathetic nervous system (SNS) activation and reduced parasympathetic

nervous system (PNS) activity, leading to elevated heart rate and blood pressure, heightened stress responses, and pre-sleep anxiety—all of which markedly impair sleep quality.[58] Patients with insomnia often remain in a persistent state of sympathetic overactivity, accompanied by increased cortisol secretion and impaired nocturnal relaxation, while reduced parasympathetic function further compromises recovery and homeostatic regulation.[59] Heart rate variability (HRV), a key biomarker of ANS balance, is consistently decreased in insomnia, reflecting diminished vagal tone and an inability to downregulate arousal at sleep onset.[60] This autonomic imbalance interacts with the hypothalamic–pituitary–adrenal (HPA) axis, forming a vicious cycle of stress hormone release and heightened cortical excitability.

Wix-Ramos et al[57] compared ANS function between chronic insomnia patients and healthy controls using wearable monitoring devices. Insomnia patients showed significantly reduced sleep efficiency and total sleep time, prolonged sleep latency, and increased wake time after sleep onset. In terms of sleep architecture, abnormalities were mainly observed during slow-wave sleep, whereas no significant differences were detected during REM sleep. Physiologically, patients exhibited elevated heart rates across all sleep stages, reduced HRV during slow-wave sleep, increased HRV during REM sleep, and heightened sweating responses. These findings indicate excessive autonomic activation manifested as tachycardia, impaired thermoregulation, and exaggerated vegetative responses during sleep. Importantly, such objective markers suggest that ANS hyperactivity is not merely a subjective perception but a measurable physiological alteration in insomnia.

Beyond ANS dysfunction, abnormalities in specific central nervous system (CNS) regions also play a pivotal role in insomnia.[61] Chronic psychological stress may impair the cerebral cortex and prefrontal regions, disrupting neurotransmitter and hormonal balance and perpetuating a state of hyperarousal.[62] Studies have reported a negative correlation between CNS excitability and insomnia, with arousal-related emotions acting as critical modulators, suggesting that both emotional regulation and neural excitability jointly contribute to insomnia pathogenesis.[63] Functional neuroimaging consistently reveals hyperactivation of wake-promoting regions such as the amygdala and anterior insula, coupled with reduced inhibitory control from the medial prefrontal cortex.[64] These alterations create a neurocognitive state biased toward vigilance, thereby maintaining difficulty in initiating and sustaining sleep.

Moreover, dysfunction of the hypothalamus and pineal gland—including reduced melatonin secretion and disrupted circadian rhythms—has been closely linked to insomnia.[65] The suprachiasmatic nucleus (SCN) of the hypothalamus, as the central circadian pacemaker, shows altered activity patterns in insomnia, impairing synchronization between internal circadian timing and the external light–dark cycle. Neuroimaging studies reveal abnormal hypothalamic–cortical circuits in insomnia patients.[66] Ding et al[67] demonstrated enhanced resting-state functional connectivity between the left hypothalamus and medial prefrontal cortex, but reduced connectivity with the right temporal cortex. Notably, the strength of these connections positively correlated with Pittsburgh Sleep Quality Index (PSQI) scores, suggesting that hypothalamic–cortical circuit abnormalities may directly underlie the onset and persistence of insomnia. Longitudinal data further indicate that disruption of pineal melatonin output contributes not only to delayed sleep onset but also to impaired sleep continuity, reinforcing the role of circadian dysregulation in chronic insomnia.

Insufficient Blood Perfusion

Insufficient blood perfusion is increasingly recognized as a significant contributor to sleep disorders. Reduced cerebral or systemic blood flow limits oxygen and nutrient delivery to neurons, thereby impairing synaptic activity, neurotransmitter homeostasis, and the functional integrity of brain regions critical for sleep regulation, including the hypothalamus, prefrontal cortex, cerebellum, and hippocampus.[68] Inadequate perfusion can directly disrupt sleep initiation and maintenance by reducing neuronal excitability in these regions, while also exacerbating hyperarousal and prolonging sleep latency. Moreover, insufficient circulation may trigger nocturnal discomfort or pain, such as leg cramps, chest tightness, and dyspnea, which increase nighttime awakenings and fragment sleep architecture.[69] Chronic perfusion deficits further compromise metabolic clearance and neuronal recovery, accelerate brain aging, and may contribute to the progression of cerebrovascular and systemic diseases, creating a vicious cycle between sleep disturbance and overall health deterioration.

Neuroimaging studies provide direct evidence linking perfusion deficits to insomnia pathophysiology. In patients with comorbid chronic insomnia and major depression, decreased blood flow in the cerebellum, vermis, right hippocampus, and left parahippocampal gyrus correlated with greater symptom severity, suggesting that hypo-perfused regions are crucial for both emotional regulation and sleep control. Functional connectivity analyses further revealed compensatory

and maladaptive network alterations: enhanced connectivity between the left cerebellum–right caudate and right hippocampus–left inferior frontal gyrus, alongside reduced connectivity with occipital and precentral regions, indicating widespread reorganization of cerebrovascular networks involved in emotion–sleep interactions.[70] Arterial spin labeling studies in patients with cerebral small vessel disease similarly showed reduced gray matter perfusion in the left hippocampus among individuals with poor sleep quality, reinforcing the notion that perfusion deficits may drive insomnia pathogenesis rather than merely reflect its consequences.[71]

Mechanistically, impaired perfusion may interfere with neurotransmitter distribution and signaling. Regions with reduced blood flow exhibit diminished GABAergic and serotonergic activity, which can exacerbate hyperarousal and disrupt NREM and REM sleep continuity.[72] Hypoperfusion may also impair hypothalamic circadian pacemaker activity and melatonin secretion, further compromising sleep timing and quality.[73] From a cognitive and emotional perspective, the prefrontal cortex and hippocampus are highly sensitive to oxygen and glucose deficits; their dysfunction contributes to impaired emotional regulation, increased stress responsiveness, and heightened vulnerability to anxiety- and depression-related insomnia.[74]

Clinically, restoring adequate cerebral perfusion has been associated with improvements in sleep quality. Interventions that enhance systemic and cerebral blood flow—including aerobic exercise, vascular-targeted pharmacotherapy, and management of cardiovascular risk factors—can reduce sleep fragmentation and improve subjective sleep satisfaction. Advanced imaging techniques such as arterial spin labeling MRI, SPECT, and PET provide valuable biomarkers for identifying high-risk individuals and monitoring treatment efficacy.[75]

In summary, insufficient blood perfusion contributes to insomnia through multiple interconnected pathways: (1) disruption of neurotransmitter balance and impairment of sleep-regulatory brain regions; (2) induction of nocturnal discomfort and pain, leading to frequent awakenings; (3) remodeling of functional brain connectivity and emotion–sleep regulation circuits; and (4) compromised metabolic clearance and homeostatic recovery. These findings underscore the importance of vascular health in sleep regulation and highlight perfusion-targeted strategies as potential therapeutic approaches for insomnia.

Acupuncture for Insomnia: Multidimensional Mechanistic Perspectives

Traditional Chinese medicine (TCM) has a long-standing history in the treatment of insomnia, with extensive clinical experience demonstrating unique therapeutic advantages. Modern studies indicate that various TCM therapies not only improve sleep quality but also exert multi-target and multi-pathway effects, including modulation of inflammatory responses, optimization of neurotransmitter signaling, and restoration of neuroendocrine homeostasis, thereby achieving holistic intervention.[76] Among these modalities, acupuncture is one of the most widely practiced and internationally recognized approaches,[2] showing notable efficacy in insomnia management. Grounded in the principle of "harmonizing yin and yang, unblocking meridians, and supporting the healthy while dispelling the pathogenic", acupuncture can comprehensively enhance physiological function. Contemporary mechanistic studies have revealed that acupuncture promotes cerebral blood perfusion, regulates the hypothalamic–pituitary–adrenal (HPA) axis, balances autonomic nervous system (ANS) activity, and upregulates inhibitory neurotransmitters such as serotonin (5-HT), thereby reducing hyperarousal, alleviating anxiety, and facilitating sleep.[19] Notably, acupuncture practice also demonstrates a high degree of individualization and methodological refinement. Han et al[77] investigated Professor Wang Fuchun's "sedation and calming" acupuncture technique, indicating that treatment during the Shen period (15:00–17:00) yields superior efficacy, while emphasizing the importance of needling depth, angle, direction, and manipulation (Figure 3). In summary, owing to its simplicity, safety, favorable patient compliance, and reliable efficacy, acupuncture has been widely applied in clinical insomnia treatment, providing a strong foundation for exploring its multidimensional mechanisms.

Regulation of Neurotransmitters by Acupuncture

Insomnia is fundamentally characterized by disrupted excitatory–inhibitory balance, primarily manifested as impaired GABAergic inhibition, serotonergic dysregulation, and excessive central arousal. Rather than reiterating these well-established mechanisms, this section focuses on how acupuncture selectively counteracts these pathological alterations.

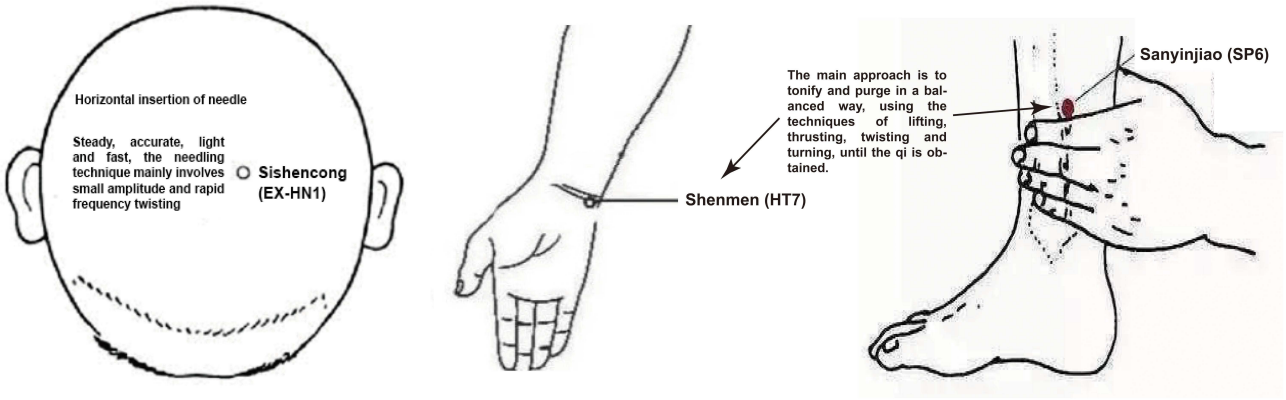

Figure 3 Schematic diagram of Professor Wang Fuchun's acupuncture treatment for insomnia.[77]

Impaired GABAergic transmission represents a core driver of hyperarousal in insomnia. Acupuncture directly targets this deficit by enhancing inhibitory neurotransmission. Experimental and clinical evidence indicates that acupuncture increases central GABA levels and upregulates GABA_A receptor expression, thereby restoring inhibitory tone and suppressing neuronal overactivity.[78–82] This restoration of inhibitory control facilitates sleep initiation and consolidation, particularly in patients with difficulty maintaining sleep.

Serotonergic imbalance further contributes to circadian disruption and mood-related sleep disturbances. Acupuncture modulates serotonergic signaling by regulating 5-HT synthesis, release, and receptor sensitivity.[83–86] Notably, this regulation appears bidirectional, normalizing both deficient and excessive serotonergic activity depending on baseline physiological states. Through this mechanism, acupuncture contributes to the stabilization of sleep–wake rhythms and the improvement of sleep continuity.

Dysregulation of other neurotransmitter systems, including dopamine and norepinephrine, also underlies heightened arousal and emotional reactivity in insomnia. Acupuncture has been shown to attenuate excessive catecholaminergic activity, thereby reducing sympathetic overdrive and promoting a neurochemical milieu conducive to sleep.[87–89] Collectively, these findings suggest that acupuncture does not act on a single neurotransmitter system but rather restores global neurochemical homeostasis, addressing the multifactorial nature of insomnia.

Acupuncture Modulation of the Nervous System

Hyperactivation of the hypothalamic–pituitary–adrenal (HPA) axis and imbalance of the autonomic nervous system (ANS) are central pathological features of insomnia, contributing to sustained physiological arousal and impaired sleep regulation. Acupuncture exerts targeted regulatory effects on both systems, thereby alleviating stress-related sleep disturbances.

Excessive HPA axis activity, characterized by elevated corticotropin-releasing hormone (CRH), adrenocorticotropic hormone (ACTH), and cortisol levels, disrupts circadian rhythmicity and sleep architecture. Acupuncture has been demonstrated to suppress this hyperactivity by downregulating CRH expression in the hypothalamus and reducing circulating cortisol levels.[90–92] Importantly, this modulation appears to restore physiological circadian patterns of cortisol secretion rather than simply inducing suppression, suggesting a normalizing rather than inhibitory effect on neuroendocrine function.

Autonomic imbalance, particularly sympathetic overactivation and reduced parasympathetic tone, further exacerbates insomnia by maintaining a state of physiological hyperarousal. Acupuncture improves autonomic regulation by decreasing sympathetic activity and enhancing vagal tone, as evidenced by changes in heart rate variability (HRV) parameters.[18,93,94] This shift toward parasympathetic dominance promotes relaxation, reduces cardiovascular and metabolic stress, and facilitates the transition to sleep.

In addition, acupuncture may influence the bidirectional crosstalk between the HPA axis and ANS. By simultaneously modulating neuroendocrine and autonomic pathways, acupuncture disrupts the self-reinforcing cycle of stress and arousal that perpetuates insomnia. This integrative regulatory effect highlights its advantage over single-target interventions.

Acupuncture Modulation of Anti-Inflammatory Substances

Chronic insomnia is increasingly recognized as a state of low-grade systemic inflammation, characterized by elevated pro-inflammatory cytokines and dysregulated immune signaling. This inflammatory milieu not only reflects sleep disturbance but also contributes to its persistence by disrupting central nervous system function. Acupuncture has emerged as a key intervention capable of restoring immune homeostasis through multi-level modulation of inflammatory pathways.

Elevated levels of cytokines such as IL-6, TNF-α, and CRP are closely associated with impaired sleep quality and altered sleep architecture. Acupuncture attenuates excessive inflammatory responses by downregulating pro-inflammatory cytokine expression while preserving physiological immune signaling.[95,96] Importantly, this effect is not purely suppressive; acupuncture appears to rebalance the immune system, maintaining cytokines within ranges that support normal sleep regulation.

At the central level, neuroinflammation disrupts neurotransmitter systems and synaptic plasticity, further aggravating insomnia. Acupuncture has been shown to inhibit microglial activation and reduce neuroinflammatory signaling in key brain regions involved in sleep regulation, including the hypothalamus and hippocampus.[97–99] This neuroprotective effect contributes to the restoration of normal neuronal function and sleep architecture.

Furthermore, acupuncture may modulate the bidirectional communication between peripheral inflammation and central nervous system activity. By influencing immune signaling, autonomic pathways, and neuroendocrine function, acupuncture interrupts the feed-forward loop linking systemic inflammation to central hyperarousal. This integrated anti-inflammatory mechanism underscores its therapeutic potential in insomnia, particularly in patients with comorbid inflammatory or stress-related conditions.

Conclusions and Future Perspectives

In summary, current evidence demonstrates that acupuncture alleviates insomnia through multidimensional regulatory mechanisms, including modulation of neurotransmitter systems, restoration of autonomic nervous system balance, attenuation of hyperactivity in the hypothalamic–pituitary–adrenal axis, and regulation of neuroinflammatory responses. These coordinated effects contribute to the reduction of hyperarousal and the improvement of both subjective and objective sleep outcomes. Compared with pharmacological therapies, acupuncture exhibits advantages in safety, tolerability, and holistic regulation, supporting its role as an effective integrative intervention for insomnia.

Future research should prioritize mechanism-driven and precision-oriented approaches. Integrating multimodal neuroimaging techniques (eg, fMRI and PET) with multi-omics strategies (such as transcriptomics, metabolomics, and microbiome profiling) will enable comprehensive characterization of brain–body interaction networks underlying acupuncture efficacy. In parallel, the application of artificial intelligence and machine learning may facilitate the identification of predictive biomarkers and the stratification of responders, thereby advancing personalized acupuncture therapy. Additionally, large-scale, multicenter randomized controlled trials with standardized protocols and objective sleep measures are essential to improve reproducibility and clinical translation. Collectively, these efforts will promote the evolution of acupuncture from an empirical therapy toward a mechanism-based precision medicine strategy for insomnia.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no conflicts of interest in this work.

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