

# 针刺治疗抑郁伴失眠障碍的临床研究进展与机制探讨

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## 摘要

抑郁症与失眠常互为因果, 形成恶性循环, 严重阻碍疾病康复。本文综述了针刺治疗抑郁伴失眠的临床进展与神经生物学机制。临床研究显示, 针刺基于“调神”理论, 能同步改善患者的客观睡眠结构与抑郁情绪, 且远期疗效稳固。机制研究表明, 针刺主要通过“多靶点、多层次”的整体调节发挥作用: (1) 调节神经递质, 平衡5-HT、NE等水平, 重塑“觉醒-睡眠”稳态; (2) 调控神经内分泌, 抑制HPA轴过度激活, 阻断应激反应; (3) 修复神经结构, 通过抗炎并激活BDNF-TrkB通路, 促进海马神经发生与可塑性恢复。针刺通过“形神同调”打破病理恶性循环, 未来应进一步聚焦于精准化治疗方案与客观评价体系的研究。

## 关键词

针刺, 抑郁症, 失眠, 神经递质, HPA轴, 神经可塑性

# Clinical Progress and Mechanisms of Acupuncture for Depression Comorbid with Insomnia

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## Abstract

Depression and insomnia frequently coexist and interact causally, creating a vicious cycle that hinders recovery. This article reviews the clinical progress and neurobiological mechanisms of acupuncture for depression comorbid with insomnia. Clinically, based on the theory of “regulating the mind” (Tiao Shen), acupuncture synchronously improves objective sleep architecture and depressive mood with stable long-term efficacy. Mechanistically, acupuncture functions through a “multi-target, multi-level” holistic regulation: (1) Modulating neurotransmitters by balancing 5-HT and NE levels to reshape “sleep-wake” homeostasis; (2) Regulating the neuroendocrine system by inhibiting HPA axis overactivation to block stress responses; and (3) Repairing neural structure by suppressing inflammation and activating the BDNF-TrkB pathway to promote hippocampal neurogenesis and plasticity. By “treating both body and mind,” acupuncture breaks this pathological cycle. Future research should focus on precision treatment protocols and objective evaluation systems.

## Keywords

Acupuncture, Depression, Insomnia, Neurotransmitters, HPA Axis, Neural Plasticity

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## 1. 引言

抑郁症(Major Depressive Disorder, MDD)是全球范围内导致致残与疾病负担加重的主要原因之一,而失眠则是抑郁症最常见的伴随症状,贯穿于疾病的前驱期、发作期及残留期。流行病学数据显示,约60%~90%的抑郁症患者伴有严重的睡眠障碍[1],且失眠往往先于情绪症状出现,被视为抑郁发作的独立预测因子[2]。临床上,抑郁与失眠之间存在复杂的“双向调节”关系:抑郁情绪导致入睡困难与早醒,而长期的睡眠剥夺又会进一步加剧认知功能受损与情绪恶化,形成难解的恶性循环。这种共病状态不仅显著降低患者的生活质量,增加了自杀风险,还导致对常规抗抑郁药物的应答率降低,使病情更易迁延难愈[3]。目前,针对抑郁伴失眠的常规治疗多采用抗抑郁药(如SSRIs)联合镇静催眠药(如苯二氮卓类)[4]。然而,长期多重用药常伴随耐药性、依赖性、日间嗜睡、体重增加及性功能障碍等不良反应,且部分患者在情绪改善后仍残留顽固的睡眠问题[5]。因此,寻求安全有效、副作用小的非药物替代疗法已成为临床关注的焦点。

针刺作为传统医学的重要组成部分,以其“简、便、廉、验”的特点在精神心理疾病的治疗中广泛应用。大量循证医学证据表明,针刺不仅能显著改善抑郁心境,更能同步调节睡眠结构,体现了中医“形神同调”的整体治疗优势。近年来,随着神经科学技术的发展,关于针刺干预抑郁伴失眠的生物学机制研究取得了长足进展。现有证据提示,针刺可能通过多靶点协同作用发挥疗效,涉及神经递质的再平衡、下丘脑-垂体-肾上腺(HPA)轴的稳态调节、神经炎症的抑制及神经可塑性的修复等多个层面。本文从临床疗效与作用机制两方面综述针刺治疗抑郁后失眠障碍的研究进展,深入探讨针刺治疗抑郁伴失眠的神经生物学机制,以期针刺的临床推广及优化方案提供科学依据。

## 2. 中医学对抑郁伴失眠障碍的认识

中医学将抑郁症归属于“郁证”范畴,而失眠则属于“不寐”范畴。二者在临床上常相兼为病,互

为因果。历代医家认为,情志不舒致郁,郁久化火扰神,神不安则不寐。《灵枢节注类编》记载:“以思虑情欲而伤脏,其精神有所之之处,执着不释,故卧不得安。”由此,提出关于情志因素导致不寐的论述。抑郁伴失眠的病机复杂,涉及多脏腑功能失调,但其核心病机可概括为“气机郁滞,阳不入阴,神不守舍”,二者在病因病机上密切相关,相互影响,共同构成了本病复杂多变的证候特点。

抑郁伴失眠的始动因素多为情志所伤,而其生理基础主要关乎肝、心二脏。《素问·举痛论》云:“百病生于气也。”肝主疏泄,调畅气机,且主藏血,血舍魂。在生理状态下,肝气条达,气血和调,则人的精神情志活动正常;夜间“人卧则血归于肝”,魂归于肝则安卧。心主神明,统领五脏六腑之大主。肝藏魂,心藏神,神魂相安,气机顺畅,卫气按时入于阴,方能成寐。正如《灵枢·营卫生会》指出:“夜半而大会……故睡眠”。在病理状态下,长期的精神抑郁导致肝失疏泄,气机郁滞。《丹溪心法·六郁》有云:“气血冲和,百病不生;一有怫郁,诸病生焉”,强调气机郁滞为诸病之始。气机郁滞导致气血运行不畅,脑神失养,临床首现情绪低落、思维迟缓等郁证表现。随着病程进展,病理产物丛生,证候虚实夹杂,呈现出复杂的演变规律。“气有余便是火”,肝郁日久化火,火热之邪上扰心神而出现肝郁化火证;亦可横逆犯脾,致脾失健运、聚湿生痰,郁火炼液为痰而上蒙清窍,加重心神不宁的痰热扰神证。思虑过度,暗耗心血,损伤脾气,以致气血化生无源,心神失养,发为心脾两虚。若病久及肾,肾阴亏虚,不能上济于心,则可致心火独亢,形成心肾不交、水火失济之证。久病入络而成瘀血,瘀阻脉络,气血运行不畅,心神失养或受扰,使病情更为胶着难愈。无论病因如何,最终必通过扰动心神而影响睡眠,如《灵枢·邪客》所言:“心者,五脏六腑之大主也,精神之所舍也”,“神安则寐,神不安则不寐”。临床上,失眠与抑郁情绪常反复发作:或先病失眠而后致肝郁,或先病肝郁而后致失眠,终致“郁寐同存”。整个病理过程构成了“因郁致寐,因寐加重郁”的恶性循环,使本病呈现出本虚标实、多脏腑同病的复杂特点。

### 3. 针刺治疗策略与临床研究进展

基于中医对抑郁伴失眠“从肝论治、调神为本”的认识,现代针灸临床发展出了多种针对性的治疗策略。大量临床研究证实,针刺不仅能改善患者的客观睡眠结构,还能有效缓解抑郁情绪,阻断“郁-寐”恶性循环。

#### 3.1 现代针灸治疗策略与理论依据

针对本病“脑神失调”的核心病理环节,现代针灸研究在传统经络理论的基础上提出了更加精准的干预策略,包括“通督调神法”、“调神固本法”与“疏肝调神法”等。其中“通督调神法”基于督脉为“阳脉之海”、并“入属于脑”的理论,通过刺激百会、神庭、大椎等督脉要穴以振奋阳气、调畅脑髓,从而改善中枢神经功能。临床与实验研究表明,该法能够有效缩短睡眠潜伏期、提高睡眠效率,其机制可能与调节中枢单胺类神经递质平衡有关[6]。“调神固本法”强调调畅气机、疏解肝郁、安宁心神,以“调神”为主;又注重健脾益气、扶阳益气、培本固肾,体现调神固本治则之精义,尤适用于情志内伤、虚实交杂之抑郁失眠共病证候[7]。“疏肝调神法”立足于肝主疏泄、与情志活动密切相关的生理功能,通过取肝经太冲、期门配合心经神门等穴,达到疏肝解郁、调畅气机、健脾养心的作用,从而改善气血濡养与神志调控,实现“形神同治”的整体调节思想[8]。三法从不同层面作用于脑-神-情志的统一系统,共同为针刺干预抑郁后失眠的机制研究提供了理论依据与临床方向。

#### 3.2. 临床治疗方式与疗效评价

针刺作为中医治疗抑郁伴失眠的主要手段,多以辨证取穴或循经取穴为基础,通过物理刺激特定穴

位以调节机体功能。大量循证医学证据表明, 针刺在改善微观睡眠结构、缓解宏观抑郁情绪以及提升远期疗效方面均具有显著优势。首先, 在改善睡眠结构方面, 多项临床研究证实了针刺的有效性。相关随机对照试验(RCT)结果显示, 相较于对照组, 针刺治疗可显著缩短抑郁症患者的入睡潜伏期(SOL), 减少夜间觉醒次数(WASO), 并延长总睡眠时间(TST) [9], 表明针刺对于入睡困难及睡眠维持障碍具有确切的改善作用。其次, 大样本研究证实了针刺疗效的稳健性与持久性。一项针对 270 例患者的高质量 RCT 研究显示, 治疗组在第 8 周时, 匹兹堡睡眠质量指数(PSQI)较基线显著下降 6.2 分; 与安慰针组和等待治疗组相比, 针刺组的 PSQI 评分分别多下降了 3.6 分和 5.1 分。更为关键的是, 这种疗效优势在随后的 24 周随访期内得以持续维持 [10], 提示针刺不仅起效确切, 且具有良好的远期疗效, 不易产生类似药物的依赖性。此外, 系统评价进一步凸显了针刺的综合优势。一项纳入 14 项研究、共 1342 例患者的 Meta 分析显示, 针刺在改善主观睡眠质量(PSQI)和缓解抑郁情绪(汉密尔顿抑郁量表, HAMD)方面, 疗效不仅优于安慰针, 且优于单纯西药治疗 [11]。同时, 针药结合模式也表现出协同效应, 研究表明, 与单独使用西药相比, 针刺联合西药治疗能更大幅度地改善患者的抑郁程度 [12], 提示针刺可能通过不同于药物的途径发挥“增效”作用。综上所述, 针刺治疗抑郁伴失眠不仅能改善客观睡眠参数, 更能兼顾情绪调节, 且在联合用药中展现出增效减毒的潜力, 是一种安全、有效的“身心同治”方案。

### 3.3. 临床研究的证据质量评价与局限性

虽然现有临床证据显示针刺在改善睡眠结构与缓解抑郁情绪方面具有显著优势, 且在 Meta 分析中展现出优于安慰针和单纯西药的潜力, 但其研究方法学仍存在一定局限性。根据 Cochrane 偏倚风险工具评价, 针刺研究的盲法实施面临巨大挑战: 由于操作的特殊性, 施术者盲法难以实现, 而受试者常能通过“得气”感识别干预, 导致盲法失败率较高, 可能引入主观期望效应偏倚。此外, 多数试验仍存在样本量较小、异质性较高(如穴位配伍与刺激强度不统一)以及客观评价指标匮乏等问题。目前的评估多依赖主观量表, 缺乏多导睡眠图(PSG)等金标准客观数据的广泛支撑。因此, 未来研究亟需构建包含多模态神经影像及客观生物学标志物的多维评价体系, 并开展大样本、标准化的临床试验以进一步验证其确切疗效。

## 4. 针刺干预抑郁伴失眠的生物学机制

抑郁伴失眠的生物学机制错综复杂, 涉及中枢神经递质失衡、神经内分泌紊乱、神经营养因子改变及神经炎症等多个环节。针刺作为一种外周物理刺激, 能够跨越血脑屏障, 通过多靶点、多通路的整体调节发挥“解郁安神”作用。

### 4.1. 调节中枢神经递质系统, 重塑“觉醒-睡眠”稳态

单胺类神经递质系统的功能紊乱, 是抑郁与失眠共病的生化基础 [1] [13]。针刺通过多靶点调节关键脑区的递质传递, 恢复兴奋与抑制的动态平衡。5-羟色胺(5-HT)既是调节情绪的“快乐递质”, 又是启动睡眠的关键因子。针刺干预可显著上调前额叶皮层及海马区 5-HT 及其合成限速酶(TPH)的表达, 增加突触间隙有效 5-HT 含量 [14]。同时, 针刺能上调突触后膜 5-HT<sub>1A</sub> 受体的表达, 这种受体的激活不仅具有抗焦虑和抗抑郁作用, 更能促进慢波睡眠(SWS)的恢复 [15], 改善“浅睡多梦”。此外, 鉴于 5-HT 是合成褪黑素的前体 [16]。针刺通过调节视交叉上核(SCN)生物钟基因(如 Clock、Per)表达、促进松果体褪黑素释放 [17] [18], 有助于重新校准昼夜节律, 纠正入睡困难及早醒, 从而阻断“因郁致寐, 因寐加重郁”。许多抑郁症患者伴有显著的焦虑与思维反刍, 处于一种病理性的“过度觉醒”状态。这种状态主要源于蓝斑核(LC)-去甲肾上腺素(NE)系统的异常激活 [19]-[21]。针刺被证实能调节 LC 活性, 抑制其向皮层和下丘脑的过度放电, 并降低下游脑区的 NE 水平 [22] [23], 通过抑制 LC-NE 系统的兴奋性, 针刺能够降低皮层觉醒水平, 缓解患者内在的焦虑紧张与思维反刍, 从而改善因“思虑过度”导致的入睡困难。此外,

抑郁症核心症状“快感缺失”源于腹侧被盖区(VTA)至伏隔核(NAc)的多巴胺(DA)投射功能低下,这导致患者日间动力不足、倦怠卧床,进而削弱了夜间的稳态睡眠驱动力[24][25]。研究表明,电针刺激可激活VTA-NAc奖赏回路,增加DA信号传递[26]-[28],从而改善情绪低落与日间疲乏;这种“抗抑郁”效应有助于打破因情绪低落而卧床难寐的恶性循环。

#### 4.2. 抑制HPA轴过度激活,阻断“应激-失眠”恶性循环

下丘脑-垂体-肾上腺(HPA)轴的持续功能亢进,是抑郁症与失眠共病的核心神经内分泌基础。长期的心理应激通过级联反应导致皮质醇(CORT)等糖皮质激素的过量释放。首先,针刺能降低激素水平,减轻神经毒性。抑郁伴失眠患者常表现为皮质醇水平持续升高并丧失正常昼夜节律(例如夜间皮质醇不降反升),这种HPA轴节律紊乱与睡眠维持障碍和情绪症状严重度相关[29][30]。高浓度的皮质醇具有神经毒性,可损伤海马神经元,削弱其对HPA轴的负反馈抑制,从而形成恶性循环并进一步损害睡眠质量与情绪调控[31]。研究证实,针刺/电针可有效抑制HPA轴的过度激活,显著降低血清皮质酮及下丘脑CRH水平[32][33],这提示针刺可通过抑制糖皮质激素的过度分泌来改善抑郁合并失眠患者中改善睡眠质量。其次,针刺能修复受体功能,重塑负反馈机制。HPA轴的稳态维持依赖于糖皮质激素受体(GR)介导的负反馈调节。在抑郁状态下,长期的高皮质醇刺激导致海马及下丘脑GR表达下调或敏感性降低(即“糖皮质激素抵抗”)[34],使机体被迫处于持续的“应激-觉醒”状态,导致难以入睡和易醒。多项研究表明,针刺可逆转这一病理改变,上调海马与前额叶皮层中GR的mRNA及蛋白表达,并增强其DNA结合活性[35][36],提示针刺可能通过恢复或调节GR介导的负反馈来重建HPA轴稳态,从而改善抑郁相关的睡眠异常。

#### 4.3. 抑制神经炎症反应,促进神经可塑性修复

长期的HPA轴亢进与心理应激会激活中枢免疫系统,引发持续的神经炎症,进而导致神经营养因子缺乏和脑结构损伤。这一病理过程被认为是抑郁伴失眠难治愈、易复发的关键机制。

抑郁伴失眠本质上是一种慢性低度神经炎症状态,多项研究表明抑郁与外周/中枢促炎细胞因子(如IL-1 $\beta$ 、IL-6、TNF- $\alpha$ )水平均升高并与症状严重程度相关[37][38]。这些促炎因子不仅可促发或加重抑郁样情绪,还能直接作用于睡眠调节相关中枢(如视前区/外周旁内分泌环路),改变神经元兴奋性与网络同步性,导致睡眠片段化、睡眠效率下降及深慢波睡眠减少[39]-[41]。针刺被证实具有显著的中枢免疫调节作用。多项研究表明,针灸可以通过调节炎症细胞信号通路的激活和减少炎症因子的释放,例如电针可以抑制CUMS大鼠海马体中的NF- $\kappa$ B/NLRP3通路,降低IL-6、IL-1 $\beta$ 、IL-18和TNF- $\alpha$ 的表达[42],并且能抑制ERK/NF- $\kappa$ B等信号、减少海马促炎因子、改善睡眠行为学指标[43]。脑源性神经营养因子(BDNF)及其受体(TrkB)是维持突触可塑性与神经元存活的关键分子底物,也被视为连接失眠与抑郁症的生物学介质[44]。在长期的抑郁应激和睡眠剥夺双重作用下,BDNF表达显著下调导致神经元树突棘密度下降、突触连接减少[45],且睡眠丧失可通过改变基因转录与胞内信号通路进一步损害BDNF依赖的突触稳定性与可塑性[46][47]。这种神经可塑性的损伤不仅可固化抑郁症状,还会削弱大脑维持正常睡眠结构(如慢波睡眠和连续睡眠)的能力[48]。针刺干预可上调海马及前额叶皮层BDNF及其受体TrkB的表达,促进转录因子CREB的磷酸化,进而启动下游基因转录程序,促进神经发生与突触重塑[49]-[51]。通过从形态学层面修复受损的神经网络,针刺不仅能缓解当前症状,更通过增强大脑的生物学“韧性”来预防复发,体现了其在治疗难治性抑郁伴失眠中的长效优势。

### 5. 总结与展望

抑郁伴失眠作为临床常见且难治的共病,其病理机制并非单一因素所致,而是涉及神经递质失衡、

HPA 轴功能紊乱、神经炎症反应及神经可塑性损伤等多维度的复杂网络交互。本文综述表明, 针刺作为一种整体调节疗法, 发挥疗效的关键在于“多靶点协同”与“多层次重塑”。从生化层面看, 针刺能够纠正 5-HT、NE 及 DA 等单胺类神经递质的传递异常, 并在调节情绪的同时恢复睡眠觉醒稳态; 从神经内分泌层面看, 针刺有效抑制 HPA 轴的过度激活, 并通过恢复糖皮质激素受体(GR)的敏感性, 阻断“应激-失眠”的恶性循环; 从微观结构层面看, 针刺通过抑制中枢炎症风暴并激活 BDNF-TrkB 信号通路, 促进海马神经发生与突触重塑, 从而逆转疾病造成的脑损伤。这种兼顾“功能调节”与“结构修复”、“治标”与“固本”的整合作用模式, 确立了针刺在治疗抑郁伴失眠中的独特优势与科学价值。

进一步分析发现, 不同针刺处方在神经生物学机制上表现出显著的“穴位-靶点”特异性(见表 1): 以百会、印堂为核心的督脉穴, 主要靶向海马与前额叶, 通过调节 5-HT 及抑制 NLRP3 炎症小体改善情绪与微环境; 配伍神门、三阴交则侧重于松果体褪黑素释放以校准昼夜节律。在针对性治疗上, 足三里、昆仑旨在激活 VTA-NAc 多巴胺奖赏回路以提振动力, 合谷、太冲则聚焦于 BDNF 信号通路以修复突触可塑性。此外, 背俞穴与期门、肾俞分别通过抑制 NF- $\kappa$ B 炎症通路和恢复 HPA 轴稳态, 从免疫与内分泌维度协同阻断病理恶性循环。

**Table 1.** Key brain regions, regulatory targets, and commonly used acupoints in acupuncture for depression comorbid with insomnia

**表 1.** 针刺干预抑郁伴失眠的关键脑区、调节靶点与常用穴位

关键脑区/解剖结构	调节靶点与生物学效应	穴位
海马、前额叶	上调 5-HT、5-HT1A 受体、TPH (合成酶)	电针百会、印堂[14]
松果体、外周血	上调 5-HT、促进松果体褪黑素释放	百会、三阴交、神门[18]
蓝斑核	调节 LC-NE 系统的功能连接	百会、神庭、本神、四神聪、三阴交、内关、神门[23]
腹侧被盖区 - 伏隔核	激活腹侧被盖区(VTA)到伏隔核(NAc)的多巴胺(DA)奖赏神经回路	足三里、昆仑、百会、印堂[28]
下丘脑	抑制了 HPA 轴活化	气海、内关、足三里等[33]
海马、下丘脑室旁核 (PVN)、垂体	上调 GR 蛋白表达, 下调了肾上腺皮层 GR、CRH 和 ACTHR 的蛋白表达	期门、肾俞、筑宾、三阴交
海马	抑制海马 NLRP 3 炎性小体激活及其介导的炎症反应	百会、印堂[42]
海马	抑制 ERK/NF- $\kappa$ B 等信号、减少海马促炎因子	心俞、肝俞、脾俞、肺俞、肾俞[43]
海马	上调 BDNF/TrkB/CREB 信号通路	合谷、太冲[50]

尽管现有研究已初步揭示了针刺的作用机制, 但该领域仍面临诸多挑战, 亟待在未来工作中深化。首先, 研究的精准化与标准化是未来的核心方向。目前关于穴位特异性及刺激参数(如频率、波形、时程)的量效关系尚显模糊, 未来研究应结合光遗传学、化学遗传学等前沿技术, 精准解析不同穴位激发的特定神经环路, 为临床制定更具针对性的标准化针刺方案提供依据。其次, 评价体系的客观化至关重要。现有的疗效评估多依赖主观量表, 未来应致力于构建包含多模态神经影像(fMRI/DTI)、多导睡眠图(PSG)及血清学标志物的多维评价体系, 以提供更直观、客观的生物学证据。此外, 拓展新兴机制探索(如“脑-肠轴”中肠道菌群与迷走神经的互作)以及关注远期疗效与复发预防, 也将是进一步阐明针刺治疗抑郁

伴失眠深层机制的重要切入点, 有助于推动针刺疗法在全球范围内的临床转化与认可。

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