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# 免疫-代谢-神经耦合视角下针刺抗抑郁的多维调控与精准治疗前景

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**【摘要】** 抑郁症是一种以情绪障碍为核心的复杂系统性疾病,其发生发展涉及免疫炎症反应失衡、代谢稳态紊乱及神经可塑性异常等多重病理过程。近年来研究提示,单一机制难以全面解释抑郁症的病理特征,多系统耦合失调可能是其重要生物学基础。针刺作为中医特色疗法,在抑郁症防治中显示出一定优势,但其作用机制尚缺乏系统整合的理论框架。本文在系统梳理针刺抗抑郁相关研究的基础上,从“免疫-代谢-神经”耦合视角出发,概述针刺对免疫炎症反应、氧化应激及能量代谢、神经可塑性及脑网络的调控证据,重点探讨其通过关键分子节点与信号通路介导的跨系统级联调节可能。进一步提出针刺或可通过重塑免疫-代谢-神经网络的动态平衡,促进系统稳态重建,从而发挥抗抑郁效应,以期阐明针刺抗抑郁的系统调控机制及临床个体化应用提供理论参考。

**【关键词】** 针刺;抑郁症;免疫炎症反应;代谢稳态;神经可塑性;脑网络功能

## Multidimensional regulation and precision therapeutic prospects of acupuncture against depression from the perspective of immunity-metabolism-nerve coupling

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**【ABSTRACT】** Depression is a complex systemic disease dominated by emotional disorders, whose occurrence and progression involve multiple pathological processes including imbalance of immune inflammatory response, disrupted metabolic homeostasis and abnormal neural plasticity. Recent studies indicate that a single mechanism cannot fully interpret the pathological characteristics of depression, and multi-system coupling dysfunction serves as a crucial biological basis. As a characteristic traditional Chinese medical therapy, acupuncture presents favorable efficacy in the prevention and treatment of depression, yet its action mechanism lacks a systematically integrated theoretical framework. Based on a systematic review of relevant studies on the antidepressant effect of acupuncture, this paper summarizes regulatory evidence of acupuncture on immune inflammation, oxidative stress, energy metabolism, neural plasticity and brain network from the immunity-metabolism-nerve coupling perspective. It mainly discusses the cross-system cascade regulation mediated by key molecular nodes and signaling pathways. Furthermore, it proposes that acupuncture may exert antidepressant effects by remodeling the dynamic balance of the immunity-metabolism-nerve network and restoring systemic homeostasis. This study aims to provide theoretical references for clarifying the systematic regulatory mechanism of acupuncture against depression and promoting its individualized clinical application.

**【KEYWORDS】** Acupuncture; Depression; Immune inflammatory response; Metabolic homeostasis; Neural plasticity; Brain network function

抑郁症是一种以持续性情绪低落、兴趣减退和认知功能障碍为主要特征的常见精神障碍,其高发病率和复发风险已成为严重威胁人类身心健康和

社会功能的重要公共卫生问题<sup>[1-2]</sup>。尽管现代医学在抑郁症的药物和心理治疗方面取得了一定进展,但临床实践中仍普遍存在起效缓慢、不良反应明显

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及疗效个体差异大的问题,充分反映其病理机制的复杂性<sup>[3-4]</sup>。

近年来,研究者逐步认识到抑郁症不仅是单纯的中枢神经系统(CNS)疾病,更是一种涉及免疫、代谢与神经调控等多系统异常的全身性疾病。随着神经免疫学、代谢组学及多组学技术的快速发展,研究逐渐突破了传统的单胺类递质假说,认识到抑郁症的发生发展与外周-中枢免疫、神经元与神经胶质细胞代谢及脑网络功能之间存在复杂而动态的相互作用。大量研究结果显示,抑郁症患者外周及中枢炎症因子水平异常升高,免疫细胞功能失衡,炎症信号通过多种途径影响神经递质代谢、神经营养因子表达及脑网络功能<sup>[5]</sup>。同时,代谢紊乱与能量代谢障碍在抑郁症中的作用逐渐受到关注,线粒体功能受损、氧化应激增强及代谢通路异常不仅能加重神经炎症反应,还可能通过影响神经元能量供给和突触可塑性,参与抑郁样行为的形成<sup>[6-8]</sup>。上述免疫、代谢与神经系统之间并非孤立存在,而是通过多层次、多通路的互作形成复杂的耦合网络,其动态失衡可能构成抑郁症的重要病理特征。

针刺作为中医学的重要组成部分,在抑郁症防治中具有悠久的临床应用历史和独特优势。现代研究表明,针刺不仅能够改善抑郁症的情绪症状,还可调节免疫炎症反应、改善代谢异常并促进神经可塑性恢复<sup>[9-10]</sup>。近年来,针灸研究正逐步走向系统整合与多学科交叉;如《针灸科学研究行动计划》所倡导的“针灸调控的系统生物学规律探索”和“临床与基础研究的互促转化”,强调从整体与动态视角解析针灸的调控机制与应用潜力<sup>[11]</sup>。然而,现有研究多集中于单一系统或单一信号通路,缺乏对不同系统之间相互关联和整体调控效应的整合。这不仅限制了我们对针刺作用本质的深入理解,也制约了其临床精准应用。基于此,本文在系统梳理针刺抗抑郁相关研究的基础上,引入“免疫-代谢-神经”耦合的整体视角,综述针刺对免疫炎症反应、代谢稳态及神经可塑性的调控作用,以期阐明机制及推动针刺在抑郁症中的精准治疗提供理论依据。

## 1 抑郁症的多维病理基础

### 1.1 免疫炎症反应失衡与抑郁的发生发展

免疫炎症反应在抑郁症的发生和发展中发挥重要作用,其核心变化为免疫炎症反应系统(IRS)过度活化,同时代偿性免疫调节系统(CIRS)受到抑

制<sup>[12]</sup>。临床研究表明,抑郁症患者外周血中多种促炎因子如白细胞介素-1 $\beta$ (IL-1 $\beta$ )、白细胞介素-6(IL-6)、肿瘤坏死因子- $\alpha$ (TNF- $\alpha$ )水平升高,而抗炎因子表达下降,调节性T细胞(Treg)数量减少,提示机体处于慢性低度炎症反应状态<sup>[13-15]</sup>。上述外周炎症信号可通过血脑屏障(BBB)<sup>[16-17]</sup>、外周神经系统(如迷走神经)<sup>[18]</sup>及下丘脑-垂体-肾上腺(HPA)轴<sup>[19]</sup>等多途径作用于CNS,进而驱动与情绪调控相关脑区胶质细胞的异常活化。研究显示,抑郁症患者在前额叶、前扣带回等脑区存在显著的小胶质细胞持续激活,其激活程度与抑郁症状严重性密切相关<sup>[20]</sup>。机制层面,小胶质细胞异常活化常伴随以糖酵解增强和线粒体功能重塑为特征的代谢重编程,从而放大促炎信号并触发炎症级联反应<sup>[21]</sup>;此外,小胶质细胞可通过上调NOD样受体热蛋白结构域相关蛋白3(NLRP3)表达,促进促炎介质生成,并诱导神经毒性A1型星形胶质细胞产生,进而导致星形胶质细胞萎缩与凋亡,削弱其对突触稳态与能量代谢的支持功能<sup>[22-23]</sup>。同时,小胶质细胞还可通过调控少突胶质细胞谱系的免疫表型与分化过程,引发皮质白质区低髓鞘化并损害结构完整性<sup>[24]</sup>。此外,研究还观察到特定的干细胞样记忆T细胞(T<sub>SCM</sub>)可迁移至肠道,通过前血小板碱性蛋白-CXC趋化因子受体2(PPBP-CXCR2)信号轴抑制微生物来源的神经活性代谢物高香草酸的生成,增强个体对应激的敏感性<sup>[25]</sup>。可见,免疫炎症反应失衡不仅是抑郁症的重要病理表现,也是连接外周变化与中枢神经功能障碍的关键环节。

### 1.2 代谢紊乱与能量代谢障碍在抑郁症中的作用

在抑郁症的病理进程中,代谢稳态受损是连接神经功能失调、免疫炎症反应与系统性疾病的重要枢纽。抑郁症患者常见的葡萄糖与脂质代谢异常及线粒体功能障碍,可导致三磷酸腺苷(ATP)生成不足、活性氧(ROS)过度产生并加重氧化应激,从而直接损害神经递质释放与突触功能<sup>[26-27]</sup>。更为关键的是,代谢紊乱可直接驱动神经炎症反应:色氨酸-犬尿氨酸通路异常激活及吲哚胺2,3-双加氧酶(IDO)上调,会增加神经毒性代谢物(如喹啉酸)生成并扰乱谷氨酸稳态,进而损害突触可塑性并诱发抑郁样行为<sup>[28]</sup>。此外,高脂饮食导致游离脂肪酸升高,可促使小胶质细胞向脂滴累积型小胶质细胞(LDAM)转化,并上调缺氧诱导因子1 $\alpha$ (HIF-1 $\alpha$ )信号,增强其对突触与髓鞘的吞噬作用,最终在成年期与青春期均可引发海马损伤及抑郁样行为<sup>[29-30]</sup>。

此外,代谢紊乱产生的部分终产物还具有潜在神经毒性,如抑郁症伴随的代谢紊乱会诱发全身性的氧化/硝化应激(O&NS)<sup>[31-32]</sup>。该过程不仅会直接损伤蛋白质,生成晚期氧化蛋白产物(AOPPs)<sup>[33]</sup>;更为关键的是,O&NS可通过改变自身抗原表位结构,使其转化为具有免疫原性的“新抗原”,从而可能打破免疫耐受并诱导异常自身免疫反应<sup>[31]</sup>。可见,代谢稳态的破坏是免疫炎性反应与神经功能异常之间的重要媒介。

### 1.3 神经可塑性障碍与脑功能异常

在抑郁症的病理过程中,大脑既是整合中枢,也是重要的驱动者。它不仅是外周免疫与代谢紊乱的靶点,还能通过影响神经可塑性、自主神经及神经内分泌等途径,反向调控外周,形成自我强化的病理闭环。

神经可塑性是大脑应对压力和调节免疫-代谢平衡的关键机制,其中脑源性神经营养因子(BDNF)发挥了核心作用。生理状态下,BDNF支持神经元存活,促进突触形成与神经发生,对应激缓冲和情绪稳定至关重要<sup>[34]</sup>。同时,BDNF及其受体酪氨酸激酶受体B(TrkB)在多种免疫细胞上表达,能调节T细胞分化并抑制巨噬细胞分泌促炎因子<sup>[35]</sup>。因此,BDNF水平下降不仅导致海马体积缩小与神经元功能缺失,还削弱了大脑对免疫与代谢稳态的调控能力<sup>[36]</sup>。当神经适应机制失调时,神经系统通过HPA轴、自主神经系统及神经递质网络调节整体或局部的免疫与代谢活动。例如,心理应激可导致HPA轴持续激活,增加糖皮质激素分泌,促进脂肪分解,诱发代谢共病;长期高水平的糖皮质激素还会导致免疫耐受,使炎性反应反馈失控<sup>[37]</sup>。因此,在抑郁症中,神经可塑性受损与神经内分泌系统过度激活,使大脑不仅失去对外周免疫与代谢稳态的调控能力,反而转变为驱动全身性病理紊乱的“引擎”,从而形成难以打破的恶性循环。

综上,抑郁症的病理生理基础可视为免疫、代谢与神经系统共同构成的动态网络失衡,任一系统的功能异常均可成为触发点,通过级联效应破坏整体稳态,形成自我强化的恶性循环;免疫激活可诱发神经炎性反应来干扰代谢平衡,代谢紊乱也会通过氧化应激与脂毒性作用加剧免疫及神经损伤;同时,HPA轴过度兴奋又会反向调节免疫反应及代谢进程。三者之间的持续双向交互,共同推动了抑郁症的病理进程(见图1)。

## 2 针刺对抑郁相关系统的调控作用

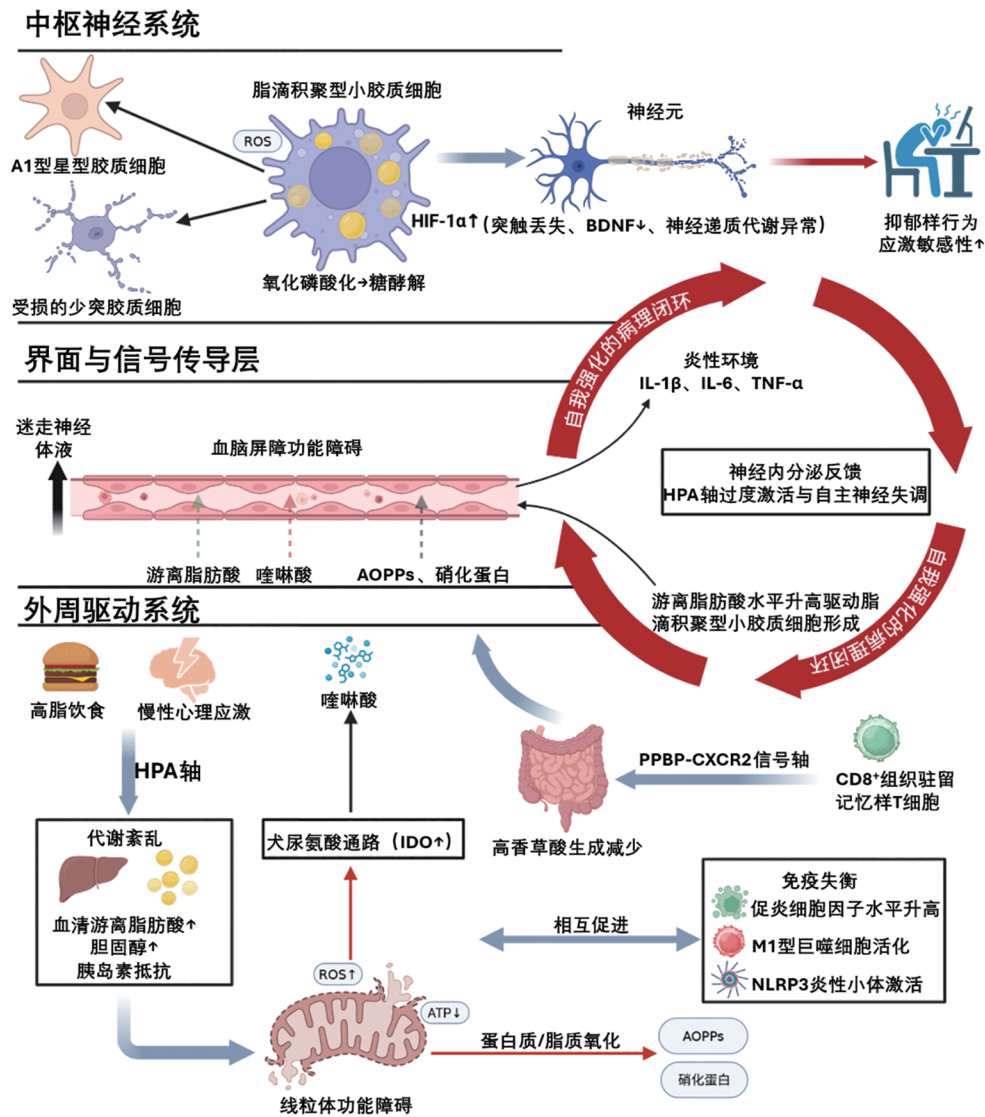
### 2.1 针刺对免疫炎性网络的调节

越来越多的研究表明,抑郁症与慢性低度炎症反应密切相关,而针刺通过多层面调节免疫炎性反应以改善抑郁症状。临床研究结果显示,针刺干预后患者外周炎性指标整体下降,促炎因子降低、抗炎因子相对上调,提示针刺具有纠正炎性反应失衡、改善慢性炎症反应状态的潜在价值<sup>[38-39]</sup>。另有研究表明,针刺可通过抑制神经炎性反应改善抑郁样行为。例如,针刺能降低慢性不可预知性温和应激(CUMS)模型大鼠海马与前额叶皮层的IL-1 $\beta$ 、IL-6、TNF- $\alpha$ 等促炎因子水平<sup>[40]</sup>。此外,电针干预还能抑制核因子- $\kappa$ B(NF- $\kappa$ B)的表达,并通过调节B细胞淋巴瘤-2(Bcl-2)/Bcl-2相关X蛋白(Bax)平衡减轻细胞凋亡<sup>[41-42]</sup>;其机制涉及降低NLRP3、凋亡相关斑点样蛋白(ASC)、半胱天冬酶-1(Caspase-1)及下游效应分子Gasdermin D蛋白(GSDMD)、高迁移率族蛋白B1(HMGB1)的表达<sup>[43-44]</sup>。同时,针刺还可抑制小胶质细胞的过度激活,从调控免疫细胞层面改善中枢炎性环境。例如,电针通过抑制嘌呤能离子通道型受体7(P2X7R)/NLRP3/IL-1 $\beta$ 通路,恢复海马小胶质细胞标记物离子钙接头蛋白-1(Iba-1)升高和星形胶质细胞标记物胶质纤维酸性蛋白(GFAP)降低的异常改变<sup>[45]</sup>。上述结果表明,针刺可能通过“抑制炎性通路-降低炎性介质活性-稳定胶质细胞反应”途径,减少神经炎性反应级联放大。

此外,针刺的抗炎效应可能通过多通路协同实现,包括抑制NF- $\kappa$ B/NLRP3通路<sup>[46]</sup>、激活海马中具有抗炎作用的G蛋白偶联受体(GPR55)<sup>[47]</sup>,以及抑制IDO介导的色氨酸降解途径,从而减轻炎性相关的神经递质代谢异常<sup>[48]</sup>,提示针刺对免疫炎性网络的调控更接近于对“炎性反应-代谢通路-神经功能”的多维干预。此外,针刺可能还涉及“脑-外周免疫器官”之间的信息传递调控。有研究指出,针刺可通过下调HMGB1/Toll样受体(TLR)4介导的“脑-脾轴”减少外周炎性负荷<sup>[49]</sup>,并影响TLR、NOD样受体(NLR)等先天免疫相关通路的基因表达<sup>[50]</sup>。因此,针刺对免疫炎性反应的影响既包括中枢局部神经炎性反应的抑制,也能通过降低外周炎性信号与重建免疫稳态,减少炎性反应对脑功能的持续扰动。

### 2.2 针刺对氧化应激和代谢稳态的恢复

氧化应激增强与线粒体功能障碍是抑郁症的重要病理环节。一方面,氧化应激可致脂质过氧化



注:ROS为活性氧,HIF-1 $\alpha$ 为缺氧诱导因子1 $\alpha$ ,BDNF为脑源性神经营养因子,AOPPs为高级氧化蛋白产物,IL-1 $\beta$ 为白细胞介素-1 $\beta$ ,IL-6为白细胞介素-6,TNF- $\alpha$ 为肿瘤坏死因子- $\alpha$ ,HPA轴为下丘脑-垂体-肾上腺轴,IDO为吡啶胺2/3-双加氧酶,ATP为三磷酸腺苷,PPBP-CXCR2为前血小板碱性蛋白-CXC趋化因子受体2,NLRP3为NOD样受体热蛋白结构域相关蛋白3。

图1 抑郁症中“代谢-免疫-神经”网络失衡的多系统交互机制示意图

Fig. 1 Schematic diagram of multisystem interaction mechanism of “metabolism-immunity-neural” network imbalance in depression

等产物积累,直接损伤线粒体结构与功能,并激活NLRP3等促炎通路<sup>[51]</sup>;另一方面,线粒体功能紊乱会引发能量代谢障碍和电子传递链异常,进一步增加ROS生成、加重氧化应激,形成恶性循环<sup>[52]</sup>。二者相互促进,共同推动神经炎症反应、细胞代谢失衡与神经元损伤,从而参与抑郁症的发生发展。针刺可通过激活核因子E2相关因子2(Nrf2)/血红素加氧酶-1(HO-1)等内源性通路发挥抗氧化作用,其深层机制在于对“氧化应激-线粒体功能障碍”这一相互耦联的病理轴进行同步、协同调控<sup>[53]</sup>。现有证据表明,这种调控覆盖多个关键节点:在上游环节,

针刺通过抑制内吞蛋白A1(Endophilin A1)降低海马ROS生成,从源头削减氧化应激负荷;与此同时,该干预亦可改善线粒体超微结构,提示其有助于减轻ROS对线粒体的直接攻击<sup>[54]</sup>。在线粒体质量控制方面,针刺上调PTEN诱导激酶1(Pink1)/帕金森蛋白(Parkin)通路,促进受损线粒体清除,从而降低氧化压力<sup>[55]</sup>。在功能重建层面,针刺通过激活腺苷酸活化蛋白激酶(AMPK)/过氧化物酶体增植物激活受体 $\gamma$ 共激活因子-1 $\alpha$ (PGC-1 $\alpha$ )轴,促进线粒体生物合成并恢复能量代谢;同时,完整高效的电子传递链可减少ROS异常泄漏,实现“促新生”与“抗氧

化”的内在统一<sup>[56]</sup>。在应对严重损伤时,针刺上调谷胱甘肽过氧化物酶4(GPX4)并抑制长链脂酰辅酶A合成酶4(ACSL4),阻断铁死亡;该过程在氧化应激与线粒体功能障碍的共同终末环节实现精准干预,从而减轻神经元损伤<sup>[57]</sup>。此外,针刺还能通过减少海马微管相关蛋白轻链3(LC3)水平来抑制过度自噬,进而保护线粒体超微结构<sup>[58-59]</sup>。在卵巢切除抑郁模型中,针刺“三阴交”可降低杏仁核的内质网应激(ER stress)与氧化应激水平,提示其对“氧化应激-ER stress-线粒体功能”网络有调节潜力<sup>[60]</sup>。值得注意的是,针刺的代谢调节作用具有系统性。电针可调节CUMS大鼠血清中葡萄糖、缬氨酸与丙氨酸等代谢物水平<sup>[61]</sup>。并能从“肠-肝-脑轴”角度改善慢性应激诱导的肝脏脂质代谢紊乱、减轻肝脏炎症反应并降低血清天门冬氨酸氨基转移酶(AST)水平<sup>[62-63]</sup>。可见,针刺通过调控氧化应激、线粒体功能及多器官代谢网络,有助于恢复抑郁症相关的能量代谢稳态。

### 2.3 针刺对神经可塑性和脑网络功能的影响

神经可塑性受损与脑网络功能紊乱是抑郁症核心症状的重要神经生物学基础。现有研究表明,针刺通过“分子-突触-环路”的多层级调节效应,促进脑功能恢复和症状改善<sup>[64]</sup>。例如,电针可提高CUMS大鼠海马组织型纤溶酶原激活物(t-PA)、BDNF和TrkB的表达改善抑郁样行为<sup>[65-66]</sup>;或通过上调BDNF/TrkB改善卒中后抑郁表现<sup>[67]</sup>。同时,针刺可提高海马与前额叶皮层中BDNF下游信号细胞外调节蛋白激酶(ERK)与环磷腺苷效应元件结合蛋白(CREB)的磷酸化水平<sup>[68]</sup>,而丝裂原活化蛋白激酶激酶6(MEK)/蛋白激酶A(PKA)的抑制剂可阻断电针对这些信号的激活及其抗抑郁效应<sup>[69-70]</sup>。研究结果显示,电针可逆转CUMS导致的前额叶皮层神经元周围网络结构(PNNs)与突触后膜的突触后密度蛋白-95(PSD-95)表达下降,同时上调突触素(SYN)、谷氨酸受体1(GLUR1)表达并增加树突棘密度<sup>[71]</sup>。在社会隔离模型中,针刺可改善海马神经元树突长度与棘密度的减少<sup>[72]</sup>。在环路和网络层面,静息态功能性磁共振成像(fMRI)研究显示,针刺可调节抑郁症患者的功能连接模式,如增加杏仁核与背外侧前额叶皮层的连接,降低其与岛叶的连接<sup>[73]</sup>。与氟西汀联合治疗时,针刺可调节皮层-纹状体奖赏回路的功能连接<sup>[74]</sup>。此外,电针还能抑制默认网络的过度激活并促进全脑网络整合<sup>[75]</sup>。除了对神经通路的调控外,针刺还影响抑郁

症相关的关键核团及其免疫微环境。例如,针刺改善外侧缰核(LHb)的胶质环境,增强BDNF/TrkB/CREB通路活性<sup>[76]</sup>,并促进星形胶质细胞增殖与活化,恢复神经可塑性<sup>[77-78]</sup>。综上,针刺通过调控相关分子通路、重塑突触结构与优化神经网络连接,为抑郁症的脑功能恢复提供了重要支持。

## 3 针刺抗抑郁的“免疫-代谢-神经”耦合调控

综合现有研究结果,针刺对抑郁症的干预表现出显著的多系统调控特征(见图2)。它不仅仅只在免疫炎症反应、代谢稳态和神经可塑性等单个系统层面产生调节效应,这些作用往往相互关联、相互促进,从而在一定程度上阻断病理过程中的级联放大效应,促进机体整体功能状态的改善。这种多系统、多靶点的调控模式使针刺在抑郁症治疗中展现出良好的整体性和稳定性,为其在复杂疾病治疗中的应用提供了理论优势。

### 3.1 关键枢纽:炎症信号、能量代谢与神经营养的交汇节点

已有研究提示,抑郁症相关病理改变常通过若干共享节点实现跨系统传递与放大。如NLRP3不仅能激活相关通路诱发神经炎症反应,还可导致线粒体功能障碍和细胞焦亡,是连接炎症反应与代谢紊乱的重要节点<sup>[42-43]</sup>。针刺对其的抑制既产生直接抗炎效应,又保护了线粒体功能,获得了双重收益。类似的共享靶点还包括NF- $\kappa$ B,作为促炎因子转录的核心调控者,其过度激活会抑制BDNF表达并加剧氧化应激<sup>[41,46]</sup>。因此,针刺对NF- $\kappa$ B通路的抑制可同时发挥抗炎与促进神经修复微环境的作用。尽管现有研究中直接揭示“跨系统因果链”的证据相对有限,但上述结果为“调控枢纽”假说提供了实验基础。

### 3.2 跨系统级联:由免疫炎症反应缓解到代谢修复与神经网络重塑

抑郁症的系统性特征使得干预效应常以级联式方式传导,针刺的改善效应在不同系统间形成有序的“促进性连锁反应”。一个典型例证是,电针通过激活Nrf2/HO-1这一内源性抗氧化通路,有效缓解海马及前额叶皮层的氧化应激<sup>[53]</sup>。氧化应激水平的降低一方面直接减轻了对线粒体的损伤,改善了能量代谢稳态;另一方面也减少了对NLRP3等炎症信号的激活,从而间接减轻了神经炎症反应<sup>[42,44]</sup>。更为重要的是,氧化还原平衡的细胞内环境是

BDNF有效合成及其下游CREB等转录因子正常运作的基础。针刺通过上游的抗氧化作用,为下游BDNF/TrkB/CREB信号的激活和突触可塑性的恢复扫清了障碍,形成了“代谢改善”到“炎症反应减轻”再到“神经修复”的连贯性促进链条<sup>[65-66,70]</sup>。

### 3.3 从局部刺激到系统稳态:外周-中枢的交互调控

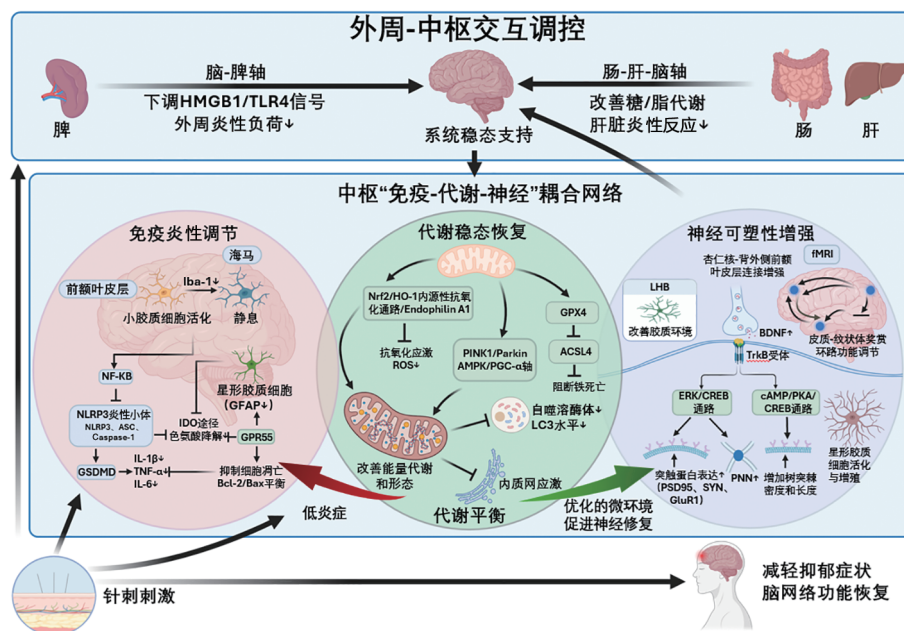
针刺作为外周刺激,通过感觉传入与中枢整合影响神经-内分泌-免疫网络,体现出“自上而下”(中枢通过神经-内分泌-免疫通路对外周炎症反应的反馈)与“自下而上”(针刺外周感觉传入引发的中枢整合)相结合的交互调控特征。在宏观系统层面,针刺调控连接外周与中枢的“生理轴系”,实现机体功能的整体协同。例如,针刺通过下调HMGB1/TLR4介导的“脑-脾轴”信号,减轻中枢炎症反应的同时降低了外周血的炎性水平,实现了免疫系统的内外协调<sup>[49]</sup>。同时,针刺通过“肠-肝-脑轴”改善慢

性应激诱导的肝脏脂质代谢紊乱、减轻肝脏炎症反应,并调节血清代谢物水平<sup>[62,79]</sup>。这表明针刺能够从整体上协调肝、肠等代谢器官与大脑之间的通讯,同步解决“外周能量代谢危机”和“中枢营养支持不足”的问题,从而优化大脑功能的恢复环境。

然而,目前有关针刺抗抑郁的“跨系统因果链”的直接证据仍相对不足,现有研究多为单系统观察或相关性推断。未来应通过多组学、多指标同步检测、因果干预验证(如通路阻断/细胞特异性操控),以及临床多模态评估等策略,系统阐明针刺在免疫-代谢-神经耦合网络中的关键作用环节与主导路径,以提升其可检验性与临床转化价值。

## 4 小结与展望

转化的直接障碍。尽管现有研究揭示了针刺效果的“穴位特异性”与“刺激参数特异性”,如不同穴位可引发特异的自主神经反射<sup>[80]</sup>,但针对不同病



注:HMGB1为高迁移率族蛋白B1,TLR4为Toll样受体4,Iba-1为离子钙接头蛋白-1,NF-κB为核因子κB,NLRP3为NOD样受体热蛋白结构域相关蛋白3,ASC为凋亡相关斑点样蛋白,Caspase-1为半胱天冬酶-1,GSDMD为消皮素D,IL-1β为白细胞介素-1β,IL-6为白细胞介素-6,TNF-α为肿瘤坏死因子-α,IDO为吲哚胺2'3-双加氧酶,GFAP为胶质纤维酸性蛋白,GPR55为G蛋白偶联受体55,Bcl-2为B淋巴细胞瘤-2,Bax为Bcl-2相关的x基因,Nrf2为核因子E2相关因子2,HO-1为血红素加氧酶-1,Endophilin A1为吞蛋白A1,ROS为活性氧,PINK1为PTEN诱导假定激酶1,Parkin为帕金森蛋白,AMPK为单磷酸腺苷依赖的蛋白激酶,PGC-α为过氧化物酶体增殖物激活受体γ辅激活因子α,GPX4为谷胱甘肽过氧化物酶4,ACSL4为长链酰基辅酶A合成酶,LC3为微管相关蛋白轻链3,LHB为外侧缰核,fMRI为静息态功能磁共振,BDNF为脑源性神经营养因子,TrkB为酪氨酸激酶受体B,ERK为细胞外信号调节激酶,CREB为环腺苷酸应答元件结合蛋白,cAMP为环腺苷酸,PKA为蛋白激酶A,PSD95为突触后密度蛋白95,SYN为突触素,GluR1为谷氨酸受体1,PNN为神经元周围网络。

图2 针刺通过“外周-中枢”交互调节重塑抑郁症相关的免疫-代谢-神经耦合网络示意图

Fig. 2 Schematic diagram of acupuncture remodeling immune-metabolic-neural coupling network related to depression via peripheral-central interactive regulation

理状态的最优治疗方案尚未系统解答。

未来研究应聚焦以下方向以突破困境:(1)解析时空动态的协同调控,通过单细胞测序、空间转录组与在体功能成像等技术,动态解析针刺干预下“神经元-胶质细胞”互作及“免疫-代谢-神经”网络的实时响应模式;(2)构建系统性的理论模型,整合多组学数据,利用人工智能与计算生物学建立量化的网络模型,以预测针对不同病理亚型的最佳干预方案;(3)推动精准临床研究,开展大规模、多中心、随机对照试验,基于免疫、代谢与影像等多维度生物标志物对抑郁症进行客观分型,并前瞻性探究针刺对各亚型的疗效。通过这些多维度的协同探索,有望揭示针刺系统性疗效的深层机制,并为明确其在现代医学体系中的应用价值,以及抑郁症精准诊疗体系构建,提供崭新理论依据与实践框架。

**利益冲突** 所有作者声明不存在利益冲突。作者陈永君为本刊编委,但未参与本文的审理。

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