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基于神经内分泌调节探讨针灸治疗神经障碍的潜在机制

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摘　要

针灸作为中医的基石，在西方医学中因其通过神经内分泌调节治疗精神障碍的潜力而得到认可。本综述探讨了神经内分泌系统在调节情绪、压力和心理健康方面的作用，重点研究了下丘脑－垂体－肾上腺轴、下丘脑－垂体－甲状腺轴、下丘脑－垂体－性腺轴、神经递质(血清素、多巴胺、γ-氨基丁酸)和皮质醇等关键组成部分。讨论了针灸对这些元素的影响，强调了其对神经内分泌轴和神经递质系统的双向调节作用。证据表明，针灸在治疗焦虑、抑郁、失眠和创伤后应激障碍方面具有疗效，展示了其作为心理健康护理辅助疗法的潜力。尽管需要进一步的高质量研究，但当前的证据支持针灸在治疗精神障碍中的作用。本综述强调了针灸通过神经内分泌调节的治疗潜力，并倡导继续研究和临床应用，以扩大精神障碍的治疗选择。

关键词

针灸，精神障碍，神经内分泌调节

Exploration of the Potential Mechanisms of Acupuncture in Treating Neurological Disorders Based on Neuroendocrine Regulation

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Abstract

Acupuncture, a cornerstone of Traditional Chinese Medicine, has gained recognition in Western medicine for its potential to treat mental disorders through neuroendocrine modulation. This review explores the neuroendocrine system's role in regulating mood, stress, and mental health, focusing on key components such as the hypothalamic-pituitary-adrenal axis, hypothalamic-pituitary-thyroid axis, hypothalamic-pituitary-gonadal axis, neurotransmitters (serotonin, dopamine, gamma-aminobutyric acid), and cortisol. The effects of acupuncture on these elements are discussed, highlighting its bidirectional modulation of neuroendocrine axes and neurotransmitter systems. Evidence suggests acupuncture's efficacy in treating anxiety, depression, insomnia, and post-traumatic stress disorder, demonstrating its potential as an adjunctive therapy for mental health care. While further high-quality research is necessary, current evidence supports acupuncture's role in mental disorders treatment. This review underscores acupuncture's therapeutic potential through neuroendocrine regulation and advocates for continued research and clinical application to expand treatment options for mental disorders.

Keywords

Acupuncture, Mental Disorder, Neuroendocrine Modulation

1. 引言

现阶段，精神健康问题构成了一个严峻的全球性挑战，影响全球约 13%的人口，并显著增加了残疾人数、医疗费用和大众经济负担[1]。抑郁症、焦虑症、精神分裂症和双相情感障碍等疾病影响着全球数百万人口，常常导致患者生活质量显著下降[1]。尽管精神疾病的治疗在精神药理学和心理治疗领域取得了显著进展，但目前精神健康治疗仍然存在诸多局限。许多患者面临着治疗效果不充分、不良副作用或治疗效果延迟的问题，这凸显了对更有效和全面治疗策略的迫切需求。

针灸的历史可追溯至 2000 年以上，应用范围十分广泛，包括对心理健康的调节。该疗法基于中医的整体观，强调心灵、身体与精神之间的和谐统一[1]。在中医理论中，精神与身体紧密相连，有着独特且深刻的认知[2]。《内经》记载："人有五脏化五气，以生喜怒悲忧恐"，清晰阐述了五脏与情志的内在联系。心主喜，心生喜悦之情；肝主怒，肝气不舒易引发愤怒；脾主思，思虑过度易伤脾；肺主忧，忧愁情绪与肺相关；肾主恐，恐惧之感源于肾。这种观点强调人体是一个有机整体，精神情志活动并非孤立存在，而是与脏腑功能相互影响。当脏腑功能失调时，可引发情志异常；反之，长期的情志过激也会损伤相应脏腑。针灸通过调整脏腑功能，恢复人体阴阳平衡，从而改善精神情志状态，为精神障碍的认识与治疗奠定了坚实理论基础，如今针灸已逐渐成为精神障碍治疗领域中一种具有潜力的辅助疗法，其主

要作用机制在于对神经内分泌系统的调节效应[3]。《素问·举痛论》中言：“百病生于气也，怒则气上，喜则气缓，悲则气消，恐则气下……惊则气乱……思则气结”，清晰地阐述了情志与人体气机的关系，长期的情志过激，如过度的愤怒、忧愁、思虑等，会导致人体气机紊乱，脏腑功能失调，从而引发一系列精神疾病。针灸疗法涉及将针具刺入身体特定穴位，以实现体内脏腑与气机的平衡[4]。通过将传统针灸技术与现代医学相结合，已发展出多种创新治疗方法，例如电针疗法和耳穴针灸[5] [6]。

近年来，针灸疗法在西方医学领域引起了日益增长的关注，尤其是其在调节神经内分泌系统方面的潜在效用，该系统在精神障碍的病理生理过程中扮演着关键角色[7]。研究揭示，针灸疗法可能对多种神经生物学途径产生影响，包括调节应激反应和情绪的下丘脑–垂体–肾上腺(HPA)轴[8]。HPA 轴功能紊乱是众多精神疾病例，如抑郁症和焦虑症的普遍特征。针灸疗法通过使 HPA 轴功能正常化，可能有助于缓解这些疾病的症状。此外，针灸疗法已被证实能够影响情绪调节中关键神经递质和神经肽的水平，如血清素、多巴胺、γ-氨基丁酸和谷氨酸[9]。这些神经化学变化可能是针灸疗法治疗效果的生物学基础，为抑郁症、焦虑症以及其他精神障碍的症状提供了缓解的可能路径[10] [11]。

将针灸纳入主流心理健康护理的做法得到了越来越多的临床证据支持，这些证据证明了其安全性和潜在益处。随机对照试验和系统评价已经考察了针灸在治疗各种精神障碍方面的有效性，包括重性抑郁障碍、广泛性焦虑障碍、创伤后应激障碍(PTSD)和失眠症[12]-[15]。虽然证据基础仍在发展中，但初步的发现表明针灸可以作为一种有效且耐受性好的辅助治疗手段，增强传统疗法的效果，并为那些对标准治疗反应不足的患者带来希望。

这篇综述旨在通过神经内分泌调节，详细检查针灸在调节精神障碍中的作用。我们将探索针灸与神经内分泌系统之间的内在联系，以揭示针灸调节内分泌系统的潜在机制，并为针灸治疗提供科学依据。通过阐明针灸发挥效果的途径，我们希望有助于更深入地理解其作为心理健康护理中补充疗法的潜力，并为这一领域的未来研究和临床实践提供信息。

2. 神经内分泌系统与心理健康

神经内分泌系统以下丘脑–垂体腺为中心，它将神经冲动转换为激素的释放，并精确调节身体的生长、发育、繁殖以及其他生命活动[16]。同时，由于神经内分泌系统紊乱导致的神经传递或激素分泌障碍与一系列精神障碍密切相关[17]。密切相关部分包括 HPA 轴、下丘脑–垂体–甲状腺轴(HPT 轴)、下丘脑–垂体–性腺轴(HPG 轴)、微生物群–肠–脑轴、心脏–脑轴等。

2.1. 下丘脑–垂体–肾上腺(HPA)轴

神经内分泌系统在调节情绪、压力和整体心理健康方面发挥着核心作用，它作为神经系统和内分泌系统之间的一个关键接口。这个复杂的网络涉及多个大脑区域、内分泌腺和激素，它们协同工作以维持稳态并响应内外刺激[18]。在其组成部分中，HPA 轴对于心理健康尤为重要，因为它管理着身体的压力反应[19]。HPA 轴由下丘脑、垂体腺和肾上腺组成。当感知到压力源时，下丘脑会释放促肾上腺皮质激素释放激素(CRH)，这会刺激垂体腺分泌促肾上腺皮质激素(ACTH)。ACTH 进而触发肾上腺产生皮质酮和皮质醇[19]。皮质醇通过动员葡萄糖、抑制非必要功能和调节免疫反应来增强身体应对压力的能力[20]。皮质醇水平升高随后通过负反馈机制抑制 CRH 和 ACTH 的分泌，使 HPA 轴在压力后恢复到基线状态[21]。然而，HPA 轴的慢性激活可能导致失调，从而促进抑郁症和焦虑症等精神障碍的发展。Daskalakis 等人的一项研究发现，创伤后应激障碍(PTSD)患者存在 HPA 轴失调和循环皮质醇水平低下的情况[22]。同样，在 Reeves 等人进行的一项研究中，广泛性焦虑障碍患者中发现交感神经系统与 HPA 轴之间的不对称性[23]。此外，Misiak 等人建议，在严重精神障碍患者中，肠道微生物可以通过几种介质激活 HPA 轴[24]。

2.2. 下丘脑－垂体－甲状腺轴(HPT 轴)

除了下丘脑－垂体－肾上腺轴(HPA 轴)外，HPT 轴也与心理健康有关。HPT 轴的功能是合成和释放甲状腺激素，这些激素对神经发育、生长和产热至关重要[25]。与促肾上腺皮质激素释放激素类似，由下丘脑合成的促甲状腺激素释放激素(TRH)到达垂体腺，并促进促甲状腺激素(TSH)的合成和释放。TSH 进入血液循环，促进甲状腺合成三碘甲状腺原氨酸(T3)和甲状腺素(T4) [25]。大量临床研究表明，甲状腺功能与精神障碍有关，包括抑郁症、早发性精神分裂症、双相情感障碍等[26] [27]。这可能是由于 HPT 轴功能障碍导致 TSH、游离 T3 和游离 T4 异常分泌引起的。

2.3. 下丘脑－垂体－性腺轴(HPG 轴)

HPG 轴是神经内分泌系统中另一个重要的组成部分，它也部分地与精神障碍有关。与 HPA 和 HPT 轴类似，HPG 轴起始于下丘脑，由弓状核和视前区释放促性腺激素释放激素(GnRH)，以周期性或脉冲式的方式进行[28]。GnRH 通过垂体门脉系统到达前垂体腺，在那里它刺激卵泡刺激素(FSH)和黄体生成素(LH)的合成和分泌。FSH 和 LH 通过血液作用于性腺，调节雌激素、黄体生成素和睾酮的产生，这些激素在个体的生殖健康、生长发育以及性别身份的维持中起着重要作用[28]。特别是雌激素的分泌和信号传导，已被发现与精神障碍，如精神分裂症、双相情感障碍和创伤后应激障碍，有很强的关联[29]。在精神分裂症患者中发现了 HPG 轴的异常，表现为女性患者雌二醇、孕酮、FSH 和 LH 浓度降低，或男性患者睾酮降低[30]。

2.4. 神经内分泌调节轴相互作用

HPA 轴、HPT 轴和 HPG 轴之间的相互作用进一步强调了它们的复杂性[31] [32]。例如，甲状腺激素通过作用于下丘脑和 Kisspeptin 间接影响 GnRH 的分泌，这些通过其受体(GPR54)激活 GnRH 神经元，是调节 GnRH 分泌的一个重要信号[33] [34]。此外，HPA 轴末端合成的糖皮质激素，如皮质醇，会抑制 GnRH 和 TSH 的分泌[35]。在应对压力时，通常优先激活 HPA 轴，而 HPG 轴和 HPT 轴则受到抑制，以便集中能量应对威胁[19]。在病理条件下，例如在抑郁症患者中，已显示男性和女性 HPA 轴活动增加伴随着 HPG 轴的减少[32]。此外，三个轴在生物体受到昼夜节律系统变化刺激时相互协调[36]。

2.5. 神经内分泌系统的其他调节轴

新兴研究已经确定了其他影响心理健康的途径，例如微生物群－肠－脑轴[37]。肠道微生物产生的短链脂肪酸、神经递质和代谢产物可以通过迷走神经系统和肠神经系统直接或间接影响大脑功能和行为[37]。有证据表明，肠道微生物的行为与一系列精神障碍，如阿尔茨海默病、痴呆、焦虑、自闭症和抑郁症，有关联[38] [39]。此外，心血管系统与中枢神经系统之间的双向调节关系被定义为心－脑轴。研究发现，心－脑功能障碍不仅会导致身体疾病，而且显著影响心理健康[40]。研究发现，心力衰竭患者更有可能出现继发性认知下降、痴呆、抑郁和其他精神障碍[41]。还表明心－脑轴将心血管疾病与阿尔茨海默病联系起来[42]。

2.6. 神经递质

神经递质是化学物质，它们在神经元之间传递信号，并在神经内分泌系统中充当桥梁，将信号从中央神经系统传递到调节激素分泌和体内稳态的内分泌腺。血清素(5-羟色胺，5-HT)，常被称为“感觉良好”的神经递质，参与情绪调节、睡眠、食欲和认知[43]。5-HT 水平的失衡与抑郁症和焦虑症等状况密切相关。许多抗抑郁药就是针对这一点，例如选择性 5-HT 再摄取抑制剂，它们增加与主要受体结合的 5-HT

量[44]。其失衡与抑郁症和焦虑症有很强的关联，选择性血清素再摄取抑制剂(SSRIs)通过增强 5-HT 的可用性来发挥作用[45]。血清素还通过促进 CRH 的释放来调节 HPA 轴。多巴胺(DA)是另一种关键的神经递质，对动机、奖赏和愉悦至关重要。多巴胺途径的失调可导致情绪障碍，如抑郁症和双相情感障碍，以及像精神分裂症这样的状况，在这些状况中，研究发现皮质下和纹状体中 DA 异常增加[46]-[48]。γ-氨基丁酸(GABA)是大脑中的主要抑制性神经递质，负责降低神经元的兴奋性并促进放松。GABA 功能障碍与焦虑障碍和其他与压力相关的状况有关[49]。谷氨酸也是一种重要的兴奋性氨基酸，它与下丘脑神经元上的离子型谷氨酸受体结合并促进 CRH 的分泌。在压力下，谷氨酸能神经活动增强，导致 HPA 轴的过度激活和高水平的皮质醇分泌，这与慢性压力和抑郁症的病理机制密切相关[50] [51]。应激激素，特别是皮质醇，对身体应对压力至关重要。虽然皮质醇对于管理急性压力至关重要，但长期暴露于高水平的皮质醇会对大脑和身体产生不利影响，包括海马体萎缩、认知功能受损和精神障碍风险增加[52] [53]。此外，昼夜节律失调或皮质醇调节失常常常导致睡眠障碍[54]。

总结来说，神经内分泌轴、神经递质和外部因素之间的复杂相互作用突显了神经内分泌系统在维持心理健康方面的重要作用。这种复杂性强调了其作为治疗精神障碍潜在靶点的潜力。

3. 针灸对神经内分泌系统的调节

针灸治疗在中国、日本、韩国以及其他亚洲国家广泛使用，并已被纳入传统医疗体系作为治疗工具。相比之下，在西方人群中，针灸治疗主要在指南中被认可为推荐治疗的补充和替代疗法[55]。一些临床证据，如随机对照试验，表明针灸在治疗精神障碍方面显示出良好的疗效和安全性，这些精神障碍包括重度抑郁症、广泛性焦虑障碍、创伤后应激障碍(PTSD)和失眠[12]-[15]。然而，这些试验的样本量有限和证据水平低，需要进一步的严谨研究来验证针灸对精神健康障碍的治疗潜力。

针灸对精神障碍的治疗效果可能归因于其调节神经内分泌系统的能力，特别是 HPA 轴。有趣的是，不同穴位的针灸对 HPA 轴具有双向调节作用。一项研究表明，针灸有助于调节 HPA 轴，电针刺激内关(PC6)穴位可以降低大鼠的 CRH 和皮质醇水平，并减轻应激反应[56]。郑等人的研究发现，电针刺激足三里(ST36)和三阴交(SP6)可以降低大鼠的 CRH、ACTH 和 CORT 水平，并减轻焦虑样行为[57]。这种效应可能是通过电针负向调节 Nesfatin-1/ERK/CREB 通路实现的。相比之下，闵等人发现，艾灸肾俞(BL23)和关元(CV4)可以改善杏仁核和 HPA 轴的功能，增加血清中 CRH、ACTH 和 CORT 的水平，并增加杏仁核和下丘脑中 CRH mRNA 的表达[58]。此外，张等人发现，电针和 43.5℃类似艾灸的刺激显著增加了大鼠 ST36 和 LI4 处的血浆 CRH 和 CORT 水平[59]。这些结果表明，不同的针灸方法和穴位具有很高的潜力，可以改善由 HPA 轴过度活跃引起的抑郁和焦虑，以及由 HPA 轴抑制引起的慢性疲劳综合症和创伤后应激障碍。针灸也被发现对 HPG 轴具有调节作用。张等人发现，重复低频电针刺激大鼠时，可以下调 GnRH 的表达，这可能是通过调节神经肽 Y 实现的[60]。同样，傅等人发现，与卵巢刺激模型中的大鼠相比，针灸显著降低了血清雌二醇和 FSH 的表达，并增加了垂体雌激素受体的表达，恢复了 HPG 轴的正常功能[61]。赵等人还发现，重复电针刺激通过刺激 HPA 轴，增加了去卵巢大鼠循环中的雌激素水平[62]。这些研究表明，针灸在调节 HPG 轴方面具有重要作用，以及与 HPA 轴的相互作用。针灸通过调节 HPG 轴，对围绝经期和绝经期精神障碍，如焦虑和睡眠障碍的治疗具有潜在价值，值得进一步研究。此外，研究还发现，针灸通过微生物群－肠－脑轴改善失眠、认知障碍、疲劳和其他精神障碍[63]-[65]。然而，研究的质量和证据水平较低，这一领域需要进一步的研究。

针灸也影响着多种神经递质的水平，这些神经递质对于情绪调节至关重要。研究表明，针灸可以增加 5-HT 和 DA 的分泌。陈等人的一项研究发现，患有自闭症的大鼠海马区 TPH1 (5-HT 合成限速酶)的表达上调，并且在这些大鼠接受针灸治疗后，行为异常得到了改善[66]。另一项研究表明，针灸可以刺激针

灸点下肥大细胞释放 5-HT，产生局部镇痛效果[67]。与 HPA 轴类似，针灸以双向方式调节 5-HT 系统。Park 等人发现，在 LI11 穴位进行针灸显著改善了小鼠的血清素性瘙痒，这归因于 5-HT2 和 5-HT7 受体的阻断[68]。同样，针灸增加的多巴胺分泌有助于改善情绪、动机和认知功能，为帕金森病、抑郁症和认知障碍等状况提供了潜在益处[69] [70]。但林等人发现，在百会(GV20)和印堂(GV29)进行针灸有效降低了纹状体、黑质致密部和前额叶皮层中的 DA 浓度，下调了多巴胺受体 D1R 和 D2R 的表达，并减轻了小鼠的刻板行为[71]。此外，针灸调节大脑中主要抑制性神经递质 GABA 的活动[72]。通过增强 GABA 的活动，针灸有助于降低神经元兴奋性，促进放松并减少焦虑[73]。这种对 GABA 活动的调节对于焦虑症患者特别有益，因为它有助于恢复兴奋性和抑制性神经传递之间的平衡，从而改善情绪调节。此外，针灸对 GABA 受体具有调节作用，因此具有抗焦虑效果[74]。进一步地，研究发现电针在减少 PTSD 小鼠海马区谷氨酸水平方面是有效的，表明其潜在的治疗作用[75]。不仅如此，针灸调节 GABA 与谷氨酸的比例，从而缓解抑郁症、原发性失眠和其他疾病[76] [77]。

4. 展望

总结来说，针灸通过调节神经内分泌机制，为治疗精神障碍提供了一个有前景的方法。通过影响 HPA 轴，针灸有助于降低皮质醇水平和减少应激反应，从而解决焦虑、抑郁、失眠和 PTSD 等状况中涉及的核心途径。此外，针灸能够增加 5-HT 和 DA 等神经递质的分泌，调节 GABA 和谷氨酸的活动，提供了一个多方面的治疗效果，可以改善情绪、缓解焦虑、促进睡眠和减轻疼痛。然而，针灸在 HPG 和 HPT 轴上的研究较少，仍需进一步研究以确定它是否可以通过其他神经内分泌途径改善精神障碍。

现有的研究虽然仍在发展中，但强调了针灸作为精神障碍综合管理中宝贵辅助治疗的潜力。针灸具有整体性，它同时关注心理健康中的生物和心理维度，与日益增长的综合医疗保健趋势非常契合。随着人们对神经内分泌途径的理解不断深入，针灸在调节这些系统中的作用为将其纳入心理健康全面治疗策略提供了有力的依据。

推动更高水平的科学研究对于加强针灸治疗效果的证据基础以及深化对其作用机制的认识具有至关重要的意义。采用标准化的协议以及开展更大规模样本的严谨临床试验，将有助于确认针灸在精神健康治疗领域中的关键作用。此外，实现针灸与主流临床实践的融合，将依赖于持续的教育投入以及东西方医学范式的相互协作。

通过将针灸纳入心理健康综合护理策略中，我们能够为患者提供更广泛的治疗选项，提升治疗的总体效果，并优化那些与精神障碍抗争患者的治疗成果。随着研究的深入和临床实践的扩展，针灸展现出成为心理健康整体治疗中关键组成部分的潜力，为不同患者群体提供缓解症状并促进健康的可能。

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