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综述

母亲童年期创伤对代际传递影响机制的研究进展

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［摘要］童年期创伤是指个体在童年期和青少年期所遭遇的创伤经历。母亲的童年期创伤经历会持续地影响下一代，对后代的躯体及精神心理健康产生影响，其中的机制涉及下丘脑-垂体-肾上腺轴、炎症因子、脑结构与功能、基因交互作用、教养方式等。该文对母亲童年期创伤对代际传递影响的发生机制进行系统梳理，为童年期创伤代际传递的预防提供参考。［中国当代儿科杂志，2024，26（2）：207-212］

［关键词］童年期创伤；代际传递；研究进展

Research progress on the mechanism of the impact of maternal childhood trauma on intergenerational transmission

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Abstract: Childhood trauma refers to trauma experiences encountered during childhood and adolescence. Maternal childhood trauma experiences have a lasting impact on the next generation, affecting their physical and mental well-being. The mechanisms involved include the hypothalamic-pituitary-adrenal axis, inflammatory factors, brain structure and function, gene interactions, and parenting styles. This paper systematically reviews the mechanisms of the impact of maternal childhood trauma on intergenerational transmission, providing insights for the prevention of intergenerational transmission of childhood trauma. **[Chinese Journal of Contemporary Pediatrics, 2024, 26(2): 207-212]**

Key words: Childhood trauma; Intergenerational transmission; Research progress

童年期创伤是指个体在儿童期和青少年期所遭遇的超过其应对能力的创伤性事件[1]，也称童年虐待、童年不良经历（adverse childhood experiences, ACEs）等，包括情感虐待、躯体虐待、性虐待、情感忽视、躯体忽视等[2]。世界卫生组织的调查显示全球1/3以上的人曾经历过ACEs[3]。2020年美国34个州211 376名成年人的一项横断面调查结果显示，57.8%的调查对象有ACEs，其中21.5%经历过3次以上[4]。国内尚没有较大规模的流行病学调查，但已有的研究数据依然值得重视，如对湖南省4 360名初中生的调查显示各类型童年期创伤的发生率为13.0%~78.6%[2]。童年期创伤可造成巨大的经济负担，2019年Meta分析显示欧洲由ACEs造成的年度总损失值约为5 810亿美元，北美该数值约为7 480亿美元，每降低10% ACEs的发生率每年可节省1 050亿美元[5]。

童年期创伤影响可持续至成年期，甚至后代。研究发现母亲经历不良的童年期经历，与其后代出现内化问题（抑郁、焦虑）和外化问题（攻击行为、违法行为）显著相关[6]，同时母亲ACEs也影响后代大脑神经发育，加重注意缺陷多动障碍症状[7]，增加发育迟缓的患病风险[8]。此外，母

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亲暴露于早年创伤，其后代发生躯体疾病（如细支气管炎[9]、肥胖[10]、过敏及哮喘[11]）的风险也显著增加。目前父亲童年期创伤对后代健康影响的相关数据较少，故本文主要对母亲童年期创伤代际传递影响后代的机制进行综述。

1 母亲童年期创伤对代际传递影响的机制分析

1.1 下丘脑–垂体–肾上腺轴失调机制

下丘脑–垂体–肾上腺轴（hypothalamic-pituitary-adrenal axis, HPA 轴）是神经内分泌的重要组成部分，在应激反应的应答和维持内环境稳态等方面具有重要作用[12]。ACEs 作为一种慢性应激，会导致 HPA 轴功能的改变，如 ACEs 会导致糖皮质激素受体（glucocorticoid receptor, GR）表达减少[13]。Lu 等[14]在一项有关抑郁症患者童年期创伤与 HPA 轴功能的研究中发现，早年创伤经历与 HPA 轴过度活动相关。另外也有研究显示经历过童年虐待，尤其是性虐待的女性，其在妊娠期表现为更高水平的皮质醇觉醒反应，童年期暴露于低经济水平的女性，在妊娠期则表现出皮质醇昼夜节律紊乱[15]。ACEs 在妊娠期间以复杂的方式影响母体的皮质醇水平[16]，并且母亲的童年期创伤性事件可预测妊娠期胎盘促肾上腺皮质激素释放激素的升高[17]。相关研究显示，母体皮质醇水平可影响新生儿杏仁核与多个大脑皮质区域的功能性连接[18]，而怀孕期间胎盘促肾上腺皮质激素释放激素的升高可引起后代大脑皮质区域变薄以及相应的认知和情绪问题[19]。

母亲童年期创伤经历亦可导致后代 HPA 轴功能的改变。美国的一项前瞻性队列研究发现母亲的创伤暴露与后代在 3 岁和 4 岁时头发中皮质醇浓度升高有关[20]。Broeks 等[21]关于母亲童年期创伤对母亲自身和婴儿皮质醇的影响研究中亦有类似结果，该研究发现母亲童年期创伤对母亲和婴儿头发皮质醇水平都有影响，但并未发现母亲头发皮质醇与婴儿头发皮质醇之间的关系。Duffy 等[22]发现母亲 ACEs 影响后代男性肾上腺体积，进而影响肾上腺的发育。

1.2 炎症机制

炎症与精神疾病的发生密切相关[23]。童年期创伤作为一种慢性创伤，目前研究[24]支持童年期创伤会触发个体炎性反应。根据 Nusslock 等[25]的神经免疫网络假说，童年早期的逆境会导致神经系统和免疫系统一系列的级联反应，最终导致全身的慢性低度炎症，从而引发一系列健康问题。既往研究显示童年期创伤与多种炎症因子关系密切，如 Meta 分析发现，童年期创伤与成年后外周血 C 反应蛋白、白细胞介素-6（interleukin-6, IL-6）、肿瘤坏死因子的升高显著相关[26]。

目前的研究主要探讨母亲或儿童自身的童年早期创伤经历对自身炎症水平的影响[27]，较少探讨母亲童年早期创伤代际影响的炎症机制。但妊娠期作为女性的一个特殊阶段，母体炎症影响后代胎儿神经发育已得到研究支持[28]。根据母体免疫激活（maternal immune activation, MIA）假说[29]，母体子宫内的炎症干扰胎儿神经发育，增加子代患孤独症谱系障碍、注意缺陷多动障碍、抽动症等神经发育类疾病的风险。目前认为母体影响胎儿大脑发育通过多种途径。首先，母体血液中的促炎细胞因子水平升高的同时，胎盘组织、羊水和胎儿大脑中的细胞因子水平也会发生改变[30]，这表明母体炎症会直接影响胎儿的炎症环境。由于促炎细胞因子在胎儿大脑发育过程中起重要作用，包括细胞分化、轴突生长和突触之间的信号转导等[31]，因此细胞因子水平的升高会影响胎儿的大脑发育，如 IL-6 被认为是产前 MIA 对后代神经发育影响的潜在介导因子[32]。在 MIA 动物模型中，Mirabella 等[33]发现产前 IL-6 升高会增加后代谷氨酸能突触密度并破坏后代海马的连接性。Rudolph 等[34]研究发现人类母体妊娠期 IL-6 平均水平与后代新生儿多个脑功能网络如背侧注意网络、凸显网络、皮质下区网络的功能连接显著相关，且与子代 2 岁期间的工作记忆能力呈负相关。也有研究发现 MIA 会干扰胎儿大脑的基因表达[35]，引起脑部解剖学结构的改变，包括总脑容量的减少[36]以及杏仁核、海马等体积的减小[37]。此外，炎症因子也可影响胎儿的神经递质系统，引起神经递质分泌增加或减少，如血清素[38]、多巴胺[39]、谷氨酰胺[40]等，进一步干扰胎儿大脑神经发育。除了直接影响胎儿大脑发育外，母亲孕期暴露于感染及炎症会引起胎儿血脑屏障的损伤，从而引起胎儿大脑的炎症，进而影响大脑发育[41]。

1.3 脑结构与脑功能机制

目前多项研究显示母亲童年期创伤可能导致后代脑结构改变。一项研究证实了此观点，该研究结果显示，与未经历地震所生的子女相比，经

历过2次地震所生子女后代双侧杏仁核体积明显较小，且右侧大脑杏仁核和海马的体积小于左侧[42]。Demers等[43]的研究同样发现母亲童年期创伤经历与后代新生儿较小的杏仁核体积有关，但并未发现双侧杏仁核体积存在差异。Moog等[44]的研究与上述研究[42-43]存在差异，该研究以80对母婴为研究对象，进行了一项前瞻性追踪研究，结果显示母亲的童年虐待经历与婴儿较小的颅内体积有关，但主要是灰质体积减小，与白质、脑脊液、海马体、杏仁核的体积无明显相关。另外该研究选择新生婴儿作为儿童大脑结构的评估期，排除了出生后的影响，这也表明这一代际传递可能在婴儿处于宫内期时就已经产生并对其随后的神经发育产生影响。Lyons-Ruth等[45]又进一步扩展了Moog等[44]的工作，结果发现母亲童年期创伤与婴儿出生后前2年大脑整体灰质和杏仁核体积较小有关。

母亲童年期创伤除影响后代脑结构变化以外，对后代脑功能也有影响。Hendrix等[46]的研究发现，母亲儿童时期暴露于情感忽视，其后代婴儿杏仁核与背侧前扣带皮质及腹内侧前额叶皮质之间的功能连接增强。2023年van den Heuval等[47]的研究发现在儿童期遭受虐待程度较严重的母亲中，胎儿杏仁核与左侧前额叶皮质和左侧前运动皮质的连接性相对较高，而与脑干、右侧前运动皮质的连接性相对较低。综上，母亲童年期创伤经历会影响后代新生儿大脑结构与功能的改变，但目前相关证据仍较少，且存在一定差异，具体机制有待进一步探究。

1.4 基因与童年期创伤的交互作用机制

表观遗传指在基因组或染色质内通过化学标记和分子修饰的方式，在不改变遗传物质序列的前提下调控基因表达，诱导机体产生一系列表型改变[48]。童年期创伤代际传递相关表观遗传学的主要机制涉及DNA甲基化[49]。首先，HPA轴相关基因甲基化参与了童年期创伤的代际传递，Bierer等[50]研究结果显示经历过大屠杀母亲的后代*FKBP5*基因第6位点的甲基化显著低于未经历大屠杀母亲的后代。一项针对*NR3C1*基因的研究表明，既往经历过暴力创伤的母亲其创伤后应激障碍症状和养育压力与外周*NR3C1*甲基化百分比降低有关[51]。Cordero等[52]研究了有人际暴力相关创伤史的母亲自身及后代*NR3C1*甲基化水平的关系，结果显示母亲*NR3C1*甲基化水平、创伤后应激障碍症状及其之间的交互作用均可预测儿童*NR3C1*甲基化水平，且母亲*NR3C1*甲基化与学龄期儿童外化行为严重程度呈负相关。其次，催产素相关基因甲基化也参与了童年期创伤的代际传递，催产素是下丘脑合成的神经肽激素，催产素在亲子互动及依恋关系的形成中发挥重要作用[53]。Gouin等[54]的纵向研究发现女性童年期暴露于生活逆境与其成年后外周血中催产素受体基因的甲基化水平变化相关，而母亲催产素编码基因启动子区甲基化的变化可预测母亲产后的母性行为[55]，从而影响后代的发展。

1.5 教养方式机制

儿童早期成长发展与家庭环境及照料者教养方式具有密切关系。母亲经历童年期创伤会对其养育能力产生负面影响，增加创伤体验传递给子女的风险，与有童年期创伤史的母亲生活在一起的儿童更有可能出现情绪和行为问题[56]。可能的途径是有童年忽视和虐待史的母亲在育儿过程中更可能以消极的方式回应子女[57]、施加更严格的养育方式[58]，且更容易形成不良的互动模式[59]。另外，研究显示童年期遭受创伤的父母其虐待自己孩子的风险升高[60]。Wang[61]的研究强调母亲情绪调节的重要性，遭受过童年期虐待史的母亲，其情绪调节更加困难，而难以调节自己情绪的母亲在育儿过程更可能使用不恰当的应对策略。此外，母亲的童年期虐待史增加了后代子女受虐待的风险，从而导致后代子女情绪调节障碍[62]，这也是童年期创伤存在代际传递的重要途径之一。总之，母亲遭受童年期创伤与不良的教养方式关系密切，而不良的教养方式不利于儿童青少年健康心理行为的发展。

2 总结和展望

童年期创伤代际传递影响的机制备受关注，其机制可能涉及HPA轴、炎症因子、基因、脑结构与功能、教养方式等。既往的大多数研究和假设更多从单一机制探讨童年期创伤代际传递的影响，缺乏整体探讨童年期创伤代际传递影响的研究，未来的研究需要系统性探讨童年期创伤代际传递影响机制，以便于更好理解机制之间的关系。另外，既往研究大多数是探讨母亲童年期创伤代际传递影响，很少涉及父亲童年期创伤的影响机制探讨，考虑父亲在后代成长过程中亦扮演重要角色，未来研究需要更加关注父亲童年期创伤的

影响机制。

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