



代谢健康的代际遗传效应： 基于母代妊娠期营养与运动的视角*

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摘要 随着中国儿童青少年代谢综合征的发病率逐渐升高, 母亲妊娠期的营养状态和身体活动对子代代谢健康的影响逐渐成为研究热点。研究表明, 妊娠期母亲不良饮食模式通过破坏胎盘功能稳态、影响宫内胎儿发育环境、调控胎儿代谢器官发育等作用途径, 显著增加子代代谢性疾病的发生风险。而妊娠期规律的身体活动可通过改善母体代谢稳态、优化胎盘结构和功能、调控表观遗传修饰等途径, 有效阻断代谢性疾病垂直传播的潜在途径。基于此, 本文综述了母亲妊娠期营养与运动对子代代谢健康的潜在交互作用以及性别特异性效应, 并深入探讨了代谢“重编程”代际调控网络的复杂性, 旨在为改善我国日益严峻的儿童青少年代谢障碍提供代际研究视角, 并为优化妊娠期代谢健康管理策略提供理论依据。

关键词 妊娠期营养, 母代运动, 表观遗传调控, 代谢编程, 代际效应

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目前, 中国已成为全球儿童青少年超重与肥胖人数最多的国家之一^[1], 预计该群体规模在 2050 年将达到 3 520 万^[2]。“健康与疾病的发育起源”(Developmental Origins of Health and Disease, DOHaD) 理论指出, 生命早期的外界刺激可能是影响胎儿及成年后发生代谢性疾病的重要因素^[3]。胎儿在宫内发育这一关键时期, 母亲的不良饮食状态将通过影响胎盘营养供给或胎儿代谢器官发育进程等途径, 损害子代的代谢健康^[4-7]。而运动作为一种安全有效的非药物干预手段, 已被证实能够通过改善母亲代谢水平^[8]、优化胎盘功能^[9]、调控表观遗传^[10-11]等途径, 有效降低子代代谢异常的发生风险。然而, 目前关于妊娠期营养与运动干预对子代代谢健康的协同效应研究仍较为匮乏。基于此, 本文系统阐述了妊娠期母亲不良饮食模式与运动干预对子代代谢系统的差异化影响。同时, 探讨母亲“营养-运动”交互作用对子代代谢健康的表观遗传修饰及代谢器官发育重塑的潜在调控机制, 以为优化妊娠期代谢健康管理策略和转化医学提供理论依据及研究方向。

1 母亲妊娠期营养失衡对子代代谢稳态的代际编程效应

妊娠期母亲营养状态通过多通路调控子代的代谢器官发育轨迹, 并可诱导代谢印记的代际传递。本部分将聚焦母亲膳食模式异常与子代代谢紊乱的内在联系, 阐述母亲妊娠期营养-表观遗传轴在代谢重编程中的重要作用。

1.1 高脂饮食 (high-fat diet, HFD)

研究表明, 妊娠期 HFD 不仅诱发母代鼠肥胖及代谢紊乱, 而且通过干扰胎盘营养转运损害胎鼠代谢系统发育^[5]。同时, 妊娠期 HFD 造成的炎性宫内环境将导致胎鼠循环系统中促炎因子水平升高^[12], 进而诱发子代鼠氧化应激损伤及肝脂肪变性等病理改变^[13]。在代谢器官肝脏中, 妊娠期 HFD 通过干扰甲硫氨酸循环诱导子代鼠发生一碳

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代谢紊乱^[14]，进而使其部分代谢关键因子发生DNA超甲基化^[15-16]，这导致子代鼠在出生后，即使进行正常饮食亦无法改善妊娠期HFD对胚胎发育时期造成的异常代谢编程。此外，HFD将损伤母代鼠乳腺组织，其分泌的低营养母乳将诱发子代鼠的代偿性摄食与“追赶性生长”现象，这进一步加剧了子代肥胖的恶性循环^[17]，形成代谢重编程的闭环效应。虽然现有研究大多聚焦于HFD对子代代谢健康的负面影响，但最新研究发现，母代鼠妊娠期HFD能够通过激活子代鼠下丘脑M1毒蕈碱乙酰胆碱受体，增强胆碱能抗炎通路，改善脂多糖诱导的脓毒症症状^[18]。这表明妊娠期HFD可能通过代谢-免疫调控网络对子代产生特定的保护作用，但其对子代长期代谢稳态的影响仍需进一步明确。

1.2 高蛋白饮食 (high-protein diet, HPD)

妊娠期HPD的补充剂量和补充时间对子代代谢健康具有差异化调控作用。早期临床研究发现，妊娠期急性HPD将诱发胎儿宫内生长迟缓，并显著升高了早产风险^[19]，早产儿代谢系统发育不全可能是成年后发生胰岛素抵抗 (insulin resistance, IR) 等代谢异常的潜在诱因。流行病学研究的局限之一是难以追踪母亲妊娠期HPD对子代代谢健康的长期影响，但模式生物的相关实验为此提供了新的机会。研究发现，母代鼠妊娠期间摄入55% HPD将引起子代鼠能量代谢调节功能缺陷和肝脏脂肪合成相关基因持续性激活，最终导致子代鼠出现糖耐量受损和肥胖发生^[7]。然而，妊娠期HPD的调控作用具有阶段特异性。妊娠晚期胎儿蛋白质需求降低，若母亲仍过量补充蛋白质可引发胎盘蛋白质异常沉积，最终导致营养转运功能障碍及供能不足^[20]。此外，妊娠期适度HPD可能使子代肥胖风险降低^[21]，这种矛盾效应可能与蛋白质来源 (如植物蛋白与动物蛋白的生物利用度差异) 或补充时间 (孕早期营养储备期，孕晚期快速生长期) 等因素密切相关。综上，妊娠期HPD的代际代谢效应呈现剂量-时间依赖的复杂动态平衡。需基于妊娠阶段特征及蛋白质生物利用度建立动态评估体系，通过胎盘功能监测与代谢组学分析实现干预窗口期和补充模式的精准调控，从而平衡母体代谢需求与胎儿发育程序的矛盾关系。

1.3 热量限制 (caloric-restriction, CR)

妊娠期CR对子代代谢健康的影响呈现出显著的复杂性与多向性，其效应高度依赖于CR的强度、时间及母亲的代谢背景。流行病学研究显示，

妊娠期CR显著增加子代成年期代谢综合征风险^[22-23]，这一现象与“DOHaD理论”相契合^[24]，提示生命早期的营养状况会对个体的长期健康产生深远影响。动物实验表明，妊娠期母代鼠20% CR通过表观遗传重编程影响子代鼠能量调控器官的发育轨迹，如下丘脑和棕色脂肪组织 (brown adipose tissue, BAT)，使子代鼠发生能量感知障碍及产热缺陷，并上调其出生后HFD导致代谢紊乱的发生风险^[25-27]。然而，CR对子代代谢的影响并非完全消极。研究表明，对患有妊娠期糖尿病或多囊卵巢综合征的母代鼠实施妊娠期60%CR可对子代鼠产生显著保护效应，这可能是由于60% CR能够有效改善母代鼠的代谢系统稳态，从而显著降低子代鼠IR和脂肪肝的发生风险^[28]。同时，该干预措施可通过调控卵母细胞DNA甲基化重编程过程，直接修复子代鼠胰岛素敏感性基因的去甲基化状态^[29]。这些发现为患代谢性疾病母亲的营养干预提供了重要的实验依据。总之，妊娠期CR对子代代谢健康的影响是一把“双刃剑”。未来研究应基于动物模型中探索不同妊娠阶段、母亲代谢表型及饮食营养构成的动态妊娠期CR策略，以建立既能缓解母亲代谢负荷又可精准调控子代发育程序的个性化营养干预体系。

1.4 低蛋白饮食 (low-protein diet, LPD)

母亲妊娠期LPD导致的子代代谢器官功能异常不仅影响个体终生的代谢稳态，还可能通过表观遗传机制实现跨代遗传效应。动物实验表明，母代鼠妊娠期LPD导致子代鼠白色脂肪组织 (white adipose tissue, WAT) 异常增生^[30]、骨骼肌线粒体功能蛋白表达下降^[31]，诱发肝脏炎症反应，即使子代鼠在后天摄入足量蛋白质仍无法降低成年期发生高脂血症的风险^[6]。同时，妊娠期LPD的代谢损伤呈现生命周期累积效应。子代鼠断乳期即可出现肥胖表型^[32]，成年期其IR和脂肪肝变性显著加重^[33]，老年期则表现为肝脏代谢代偿能力丧失及抗氧化防御系统崩溃^[34]。重要的是，母代妊娠期LPD的代际效应不仅局限于子一代，还可通过卵母细胞甲基化重编程将代谢异常表型传递至子二代^[35-36]。这一系列研究结果揭示，母代妊娠期LPD可对子代乃至跨代个体的代谢健康产生深远而不可逆的损害，凸显了妊娠期营养干预在打破代谢性疾病代际传递中的关键作用。

1.5 微量元素和维生素失调

作为维持生理功能的必需营养素，母亲在妊娠

期间微量元素和维生素稳态失衡或可成为子代代谢综合征发生的潜在风险因素。大量动物实验表明, 母代鼠在妊娠期缺乏铁、锌、铜、硒等必需元素, 易导致胎鼠宫内生长受限^[37]、早产风险升高^[38]及氧化应激加剧^[39], 其中锌缺乏引发的代谢异常具有不可逆性^[40]。另一方面, 微量元素的过度补充同样存在风险。临床研究表明, 孕妇铁过量与新生儿免疫损伤密切相关^[41], 碘过量 ($>500\text{ }\mu\text{g/d}$) 则可能抑制胎儿甲状腺功能并损害BAT产热能力^[42], 但目前孕妇在妊娠期间的碘摄入安全上限仍缺乏明确数据^[43]。此外, 维生素的协同调控效应更为复杂。维生素A通过视黄酸受体信号通路参与子代脂质代谢重编程, 其妊娠期补充剂量需严格控制在胚胎发育安全阈值内^[44-45]; B族维生素作为单碳代谢的核心辅因子, 通过调控S-腺苷甲硫氨酸合成, 影响DNA甲基化水平, 直接影响子代代谢器官可

塑性^[46-48]; 维生素C作为TET酶辅因子, 其缺乏将干扰DNA去甲基化过程, 进而导致生殖细胞表观遗传记忆异常及跨代代谢紊乱^[49]; 维生素D则可通过Wnt/ β -catenin信号通路调控胎盘发育及子代代谢器官功能^[50-51]。值得注意的是, 营养素间的协同效应可能放大或抵消单一元素的代谢影响, 这种动态平衡机制提示妊娠期营养干预需突破传统“单一营养素补充”模式, 应强调营养素之间网络化的协同调控作用。

综上所述, 母代妊娠期营养模式对子代代谢健康的代际效应已被广泛研究, 其作用网络涵盖胎盘物质转运、代谢关键基因的表观遗传重编程及代谢器官发育异常等重要通路(图1)。这些发现不仅拓展了发育源性代谢疾病干预的理论边界, 而且从转化医学视角为构建基于母亲营养调控的代际代谢疾病防控体系提供了分子靶标与策略框架。

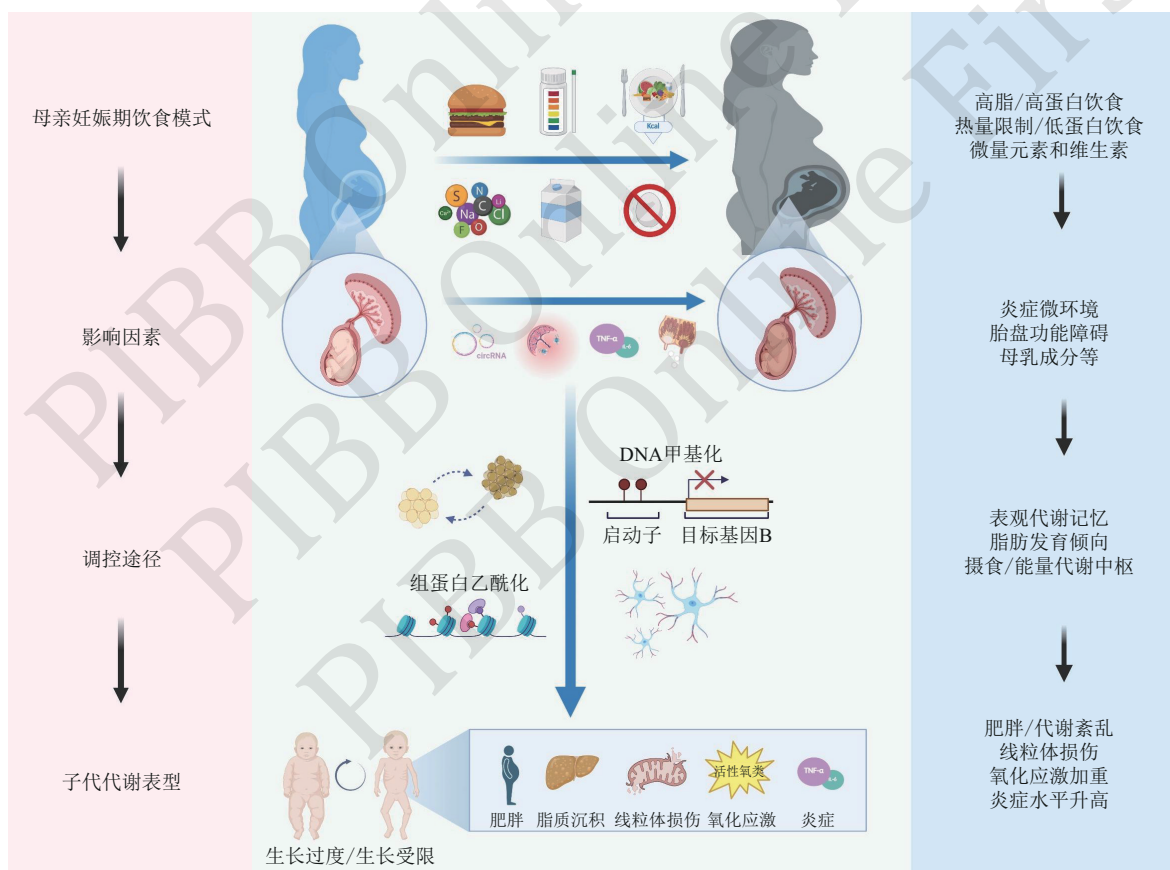


Fig. 1 Summary diagram of the mechanisms by which maternal dietary patterns during pregnancy affect the metabolic health of the offspring (created with BioRender)

图1 母亲妊娠期饮食模式影响子代代谢健康的作用机制总结图 (由BioRender绘制)

2 母代运动重塑子代代谢水平的多维途径

运动作为最具循证医学支持的健康干预策略,通过多靶点、多通路机制发挥机体功能调节作用。母代运动的系统研究始于20世纪60年代,其科学定义特指女性在孕前及妊娠期实施的身体活动行为^[52]。早期研究主要聚焦于妊娠期运动安全性评估,重点关注运动强度与胎儿宫内发育参数(如胎心率、生物物理评分)的剂量-效应关系。近年来,母代运动的相关研究从单纯安全性验证的研究范式转变为深度解析母代运动对子代代谢系统的长期健康效应及其分子机制。本部分将系统阐述母代运动对子代代谢系统的远期编程效应及关键生物学机制。

2.1 改善母亲自身代谢水平

母亲自身代谢水平失衡是诱发子代发生代谢紊乱的重要诱因。与正常妊娠期孕妇相比,妊娠期肥胖孕妇表现出循环促炎因子水平升高、氧化应激增强、线粒体自噬功能障碍和妊娠期综合症发生率高病理改变^[13, 53-54],这些因素都间接对生长中的胎儿产生负面影响。并且,肥胖孕妇体内存在的高胰岛素、瘦素和胰岛素样生长因子1等可过度激活胎盘中的mTOR信号转导,进而增强蛋白质合成及营养转运效率,最终导致胎儿营养供应过剩,促进其宫内过度生长^[55]。这些发现提示,母体肥胖可能通过多重机制对子代健康造成显著影响。母代运动可通过改善母亲妊娠期代谢状态,最终有效阻断母源性代谢异常的垂直传递。临床研究证实,孕妇进行150 min/周中等强度的有氧运动可显著降低其妊娠期糖尿病(gestational diabetes mellitus, GDM)和高血压的发生率,并有效抑制胎儿的过度生长^[8, 56]。动物实验同样表明,妊娠期运动可通过改善母代鼠的GDM状态,显著降低子代鼠发生肝脏代谢功能障碍的风险^[57]。在肥胖母代鼠模型中,妊娠期运动通过改善其血糖水平和能量消耗,从而有效防止胎鼠宫内过度生长^[58],并逆转母体肥胖诱发的子代成年期血管内皮功能障碍^[59]。这表明母亲和子代都受益于妊娠期间的身体活动,强调了妊娠期运动在促进子代长期健康中的重要性。值得注意的是,即便对于未患有GDM或肥胖等代谢综合征的健康母亲,妊娠期规律运动同样能够降低其子代儿童期发生肥胖的风险^[60]。母代运动不仅改善母亲自身代谢水平,直接缓解相关的病理状态,而且通过优化母婴间的代谢信号传递,改

善了子代的代谢健康。这不仅加深了对运动介导的代际健康效应传递机制的理解,更为防控代谢性疾病低龄化趋势提供了一种创新性的干预思路,具有重要的公共卫生意义和临床转化价值。

2.2 优化胎盘结构和功能

胎盘作为连接母婴的纽带,在母婴之间的代际“通讯”中发挥关键作用^[61]。母代运动通过调控胎盘物质交换速率、胎盘因子分泌和代谢信号转导等,有效维持或优化宫内环境的代谢稳态,为子代代谢健康发育奠定基础。研究表明,母代鼠在妊娠期进行自主转轮运动,可显著增加胎盘超氧化物歧化酶3(superoxide dismutase 3, SOD3)的分泌。SOD3通过与胎鼠肝脏中的维生素D受体结合,激活其肝脏中的AMPK-IDH- α KG-TET信号通路,从而促进子代鼠肝脏葡萄糖代谢相关基因的表达^[62]。而母代鼠运动导致的胎盘局部缺氧环境将促进爱帕琳肽的分泌,该小分子可透过胎盘屏障进入胎鼠循环系统,促进子代鼠骨骼肌*Ppargc-1 α* 基因启动子的DNA去甲基化,并抵抗HFD导致的代谢障碍^[9]。此外,脂联素(adiponectin, ADPN)是一种响应运动应激的脂肪因子,在胎盘的营养物质转运发挥重要调控作用^[63]。母代鼠在妊娠期间进行中等强度的游泳运动可能通过恢复ADPN介导的胰岛素敏感性,调节母代鼠血清瘦素和炎症因子水平,从而有效降低子代鼠发生肥胖的风险^[64]。作为一种新型因子,鸢尾素(Irisin)参与全身代谢调节^[65]。该因子不仅是运动介导代谢获益的关键信号分子,还通过促进胎盘滋养层分化和胎盘发育参与宫内胎儿发育进程^[66]。然而,妊娠并发症(如子痫前期和GDM)与循环Irisin水平较低相关^[67],这表明Irisin可能介导因妊娠并发症引起的胎盘功能受损。尽管目前尚未建立母亲运动介导胎盘Irisin水平升高与子代代谢健康改善的直接因果关联,但该分子在调控胎盘发育及代谢编程中的双重作用,使其成为介导代际代谢调控的潜在分子靶点。

另一方面,胎盘血管网络的重塑可能是母代运动促进子代代谢健康的又一重要途径。研究表明,母代鼠在妊娠期接受低强度的有氧运动干预,可激活胎盘AMPK信号通路,上调血管生成因子的表达,从而提高胎盘血管网络的密度和营养物质的转运能力^[58]。这种结构与功能上的优化不仅能够防止胎鼠在宫内过度生长,还能提高其在代谢压力环境(如母亲妊娠期HFD)下维持糖脂代谢稳态的

能力^[9]。目前, 有关母代运动如何通过重塑胎盘结构与功能, 发挥对子代代谢健康的改善作用的相关研究仍然非常有限。未来需要进一步探索母代运动介导的胎盘因子分泌和胎盘功能变化对促进子代代谢健康的具体作用机制, 以便深入揭示胎盘效应与子代代谢健康之间的关联。

2.3 调控表观遗传修饰

宫内发育期是生命程序启动的关键时间窗口, 母代运动可通过表观遗传重编程机制, 在子代代谢器官中建立代际代谢记忆。已有研究表明, 母代鼠接受中低强度跑台运动可降低子代鼠骨骼肌 *Ppargc-1a* 基因启动子区域的 DNA 甲基化水平, 增强其骨骼肌线粒体生物发生相关基因的表达, 从而有效改善子代长期 HFD 所致的骨骼肌代谢功能障碍^[68]。同时, 母代运动通过调控 *Prdm16* 基因启动子区域 CpG 位点的 DNA 去甲基化, 显著促进了子代鼠的 BAT 生成以及 WAT 向 BAT 的转化^[9]。最新的研究表明, 母代运动可上调脂肪因子 SERPINA3C 的表达与分泌, 调控 Cathepsin G/Integrin b1/PI3K/OGT/TET1 信号轴, 促进胎鼠脂肪前体细胞 *Klf4* 基因启动子区域的 DNA 去甲基化, 从而有效缓解母代鼠 HFD 诱导的子代鼠脂肪组织炎症与糖脂代谢紊乱^[11]。此外, 前期研究表明, 母代运动通过促进母代鼠肝脏维生素 C 的合成与分泌, 重编程子代鼠骨骼肌 *Slc23a2* 基因的 DNA 甲基化水平, 提高了子代鼠的骨骼肌线粒体生物发生和氧化型纤维的分化倾向^[10]。这些发现不仅丰富了对母代运动代际代谢调控机制的认识, 也为从生命早期预防代谢性疾病、改善子代长期健康状况提供了新的理论依据与干预策略。遗憾的是, 目前有关表观遗传是否可以跨代遗传仍存在争议, 尽管前期的研究表明, *Slc23a2* 基因 DNA 甲基化位点的跨代遗传可能是介导母代运动代际提高子代耐力表现的潜在机制^[10], 但仍需进一步探究母代运动跨代调控子代健康的可能。

2.4 改变母乳成分或肠道菌群

母代运动对子代代谢健康的调控效应不仅局限于宫内发育阶段, 更可通过产后的母乳中生物活性物质传递以及肠道菌群的重塑, 实现对子代代谢稳态的持续调节。研究表明, 母代鼠在产前的跑台运动可显著增强产后母乳中 3'-唾液乳糖 (3'-sialyllactose, 3'-SL) 的合成与分泌, 该低聚糖通过提高子代鼠的胰高血糖素样肽 1 的释放水平, 从而改善其胰岛 β 细胞的功能储备以及外周组织的胰

岛素敏感性^[69]。这表明 3'-SL 可能是代谢性疾病早期干预的重要潜在靶点。在微生物-代谢轴调控层面, 母代运动引起子代鼠体内多种代谢物的丰度改变, 其主要富集于丁酸代谢相关通路, 可特异性调控糖异生相关基因的表观遗传修饰状态, 形成代谢记忆效应, 从而显著改善子代鼠的葡萄糖代谢能力^[70]。此外, 母代运动还能够有效逆转 HFD 引起的母代鼠菌群失调, 并通过“菌群-肠-肌肉轴”促进子代鼠骨骼肌线粒体生物发生, 提升能量代谢效率^[71]。同时, 妊娠期运动干预还能增加子代鼠肠道内短链脂肪酸产生菌的相对丰度, 促进丁酸等关键代谢物的生成, 进一步增强肠道糖异生能力并改善外周组织的胰岛素敏感性^[72]。这种代谢保护效应具有显著的持续性, 即便在子代断奶后, 仍可稳定地维持菌群生态位结构。

2.5 妊娠期运动指导的全球共识与区域差异

根据最新国际指南及专家共识, 妊娠期身体锻炼被广泛推荐为促进母婴健康的重要措施。美国妇产科学会 (American College of Obstetricians and Gynecologists, ACOG) 建议健康孕妇每周至少分散进行 150 min 中等强度有氧运动, 并强调妊娠前已建立高强度运动习惯的孕妇可酌情调整运动形式及强度, 而非完全停止^[73]。中国《妊娠期运动专家共识 (草案)》与之类似, 建议无禁忌证的孕妇自妊娠 14 周后开展 5 d/周、30 min/次的中等强度运动, 涵盖有氧运动及抗阻运动, 同时严格规避身体接触性运动、跌倒风险项目及仰卧位运动, 以减少静脉回流障碍及低血压风险^[74]。欧洲妇产科委员会 (European Board and College of Obstetrics and Gynaecology, EBCOG) 则提倡将中等至高强度有氧运动与肌肉强化训练相结合, 并支持习惯性高强度运动者于妊娠期及产褥期在医学监督下持续进行^[75]。尽管流行病学研究提示妊娠晚期规律高强度运动 (如跑步、举重) 对多数健康孕妇具有安全性^[76], 但妊娠期间发生的解剖学和生理变化, 可能会使孕妇及其胎儿在进行高强度运动和极限运动时面临受伤的风险, 故超指南强度运动需在专业人员监护下实施。另外, 各国指南对运动强度的量化标准存在显著差异: ACOG 采用主观评估范式, 通过“谈话测试”或 Borg 自感用力度量表 (RPE 12-14 区间) 界定中等强度^[77]; 加拿大指南采用混合评估模式, 将目标心率区间 (最大心率的 60%~80%) 与对话测试相结合^[78]; 中国共识则以心率储备的 60%~80% 作为客观指标^[74]。在禁忌证管理

方面,各机构均将严重心肺疾病、子痫前期、宫颈机能不全等列为绝对禁忌,但ACOG特别指出卧床休息无益于预防早产,反而增加血栓风险。此外,ACOG与EBCOG均强调需规避高温环境运动及潜水等高危项目,而中国指南额外限制海拔1 500 m以上地区的运动。总体而言,国际共识在核心推荐上趋同,但在具体执行细节(如单次时长、强度量化)及禁忌证管理上存在区域性差异,提示临床实践中需结合个体化风险评估、文化背景及医疗资源配置进行综合决策。

综上所述,母代运动构建了贯穿从宫内发育至出生后阶段的全方位代谢保护体系,通过“母体-胎盘-表观遗传”等多级联动网络,持续改善子代糖脂代谢稳态,为代谢性疾病的早期防控开辟了新

的研究方向(图2)。但目前相关研究大多基于动物实验展开,将这些成果转化到临床实践仍面临诸多阻碍。此外,受限於动物与人体生理结构和代谢机制的差异,加之临床试验需考虑伦理、样本规模等复杂因素,致使母代运动干预的精准方案,如最佳运动时机、运动强度等,难以有效应用于临床。同时,不同调控途径间协同作用机制的研究,多停留在实验模型阶段,距离指导临床实践仍有较大差距。因此,未来研究一方面要在动物实验基础上,积极开展大样本、多中心的临床试验,明确母代运动干预的最佳时机与强度,另一方面要深入探索不同调控途径间的协同作用机制,搭建基础研究与临床应用的桥梁,为代谢性疾病的早期防控制定更科学、高效的干预策略。

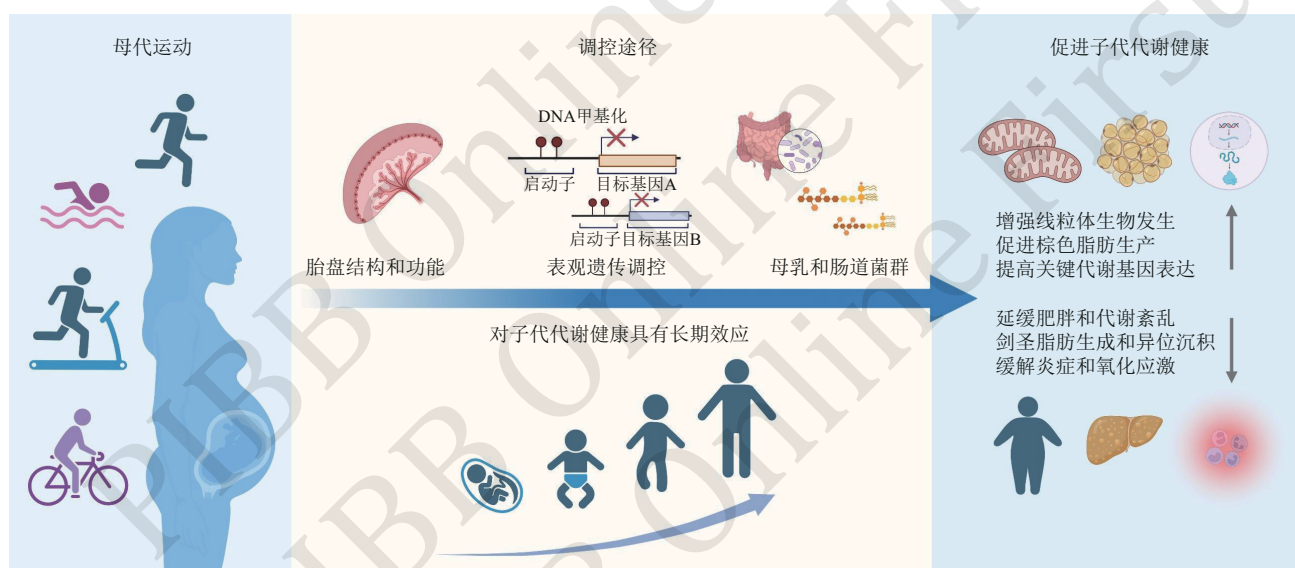


Fig. 2 Regulatory pathways of maternal exercise intervention on offspring metabolic health (created with BioRender)

图2 母代运动干预对子代代谢健康的调控路径图(由BioRender绘制)

3 母代运动与妊娠期营养的交互作用

妊娠期母亲营养-运动协同干预可能通过表观遗传重编程与代谢器官对话,动态调控子代发育编程。当前研究亟需突破单一干预范式,构建基于代谢弹性评估的动态适配模型,为跨代代谢疾病防控提供转化医学新范式。

3.1 营养-运动的协同干预与临床转化探索

近年来,母代营养与运动的协同效应逐渐成为代谢代际调控领域备受瞩目的前沿研究热点。过往研究表明,单一干预手段(如仅饮食控制或增加运

动量)虽能在一定范围内改善子代代谢表型,但其效果常受限於妊娠干预窗口期及单一调控形式。值得注意的是,现实妊娠环境往往存在复合型代谢挑战,即母亲长期暴露於营养失衡与久坐行为的双重代谢负荷中,加剧了母亲妊娠期的代谢负担。在此背景下,母亲营养-运动联合干预可能展现出更显著的协同优势。临床研究表明,针对特定代谢表型(如肥胖或GDM)母亲设计的个性化饮食-运动干预方案,如地中海饮食结合中等强度有氧运动,对子代远期肥胖风险的防控效果较单一干预形式提升40%~60%^[79]。这种协同效应本质上源于营养代谢

与能量代谢通路的双向相互作用, 即营养干预重塑母亲代谢微环境, 而运动刺激则增强代谢适应弹性, 两者通过表观遗传重编程共同优化子代代谢轨迹。

3.2 母胎代谢平衡的阈值效应: 营养匮乏状态下的干预策略革新

虽然已有研究在探索母代运动与营养联合干预的协同效应, 但母亲在特定生理状态下的代谢调控机制目前尚不清楚。特别是在母体营养匮乏的病理状态下, 运动干预引发的代谢效应是否呈现双向调节特性, 这一科学问题亟待深入探讨。从分子机制层面推测, 适度运动可能通过激活 AMPK/mTOR 信号通路, 提升母亲线粒体氧化磷酸化效率, 进而将有限的营养底物进行优先级分配, 保障胎儿的生长需求; 与此同时, 胎盘组织是否能够通过血管新生机制, 形成具有代偿功能的“代谢缓冲区”, 以缓冲母体能量供给不足带来的影响, 亦同样值得关注。另外, 运动干预的潜在风险边界仍需重点关注。当运动强度超越母体代谢储备阈值时, 母体骨骼肌对营养物质的竞争性摄取可能打破母胎间的营养平衡。目前, 这一现象在母体营养摄入受限情况下的普遍性尚未得到系统性探究。总之, 母婴代谢健康的未来研究应着重构建运动-营养相互作用的动态阈值模型, 并结合多组学监测技术, 深入解析母亲妊娠期运动-营养干预策略调控胎儿代谢系统发育的生理机制; 同时, 明确胎盘营养转运蛋白的表达动态是否可作为评估运动干预效果的实时生物标志物。对上述科学问题的系统性研究, 不仅有助于揭示生命早期代谢编程的内在规律, 更为临床制定个体化孕期运动与营养干预策略提供理论支撑, 从而在保障母胎健康的同时, 推动围产期医学领域研究的创新发展。

4 总结与展望

妊娠阶段是胎儿代谢网络构建的重要可塑期, 母亲的饮食模式与生活方式通过表观遗传调控、氧化还原稳态、代谢器官发育重编程等机制, 诱导胎儿基因表达谱、细胞功能以及器官代谢通路的适应性重塑, 对胎儿宫内发育进程产生深远影响。母源性不良膳食暴露不仅直接损害胎儿发育阶段的代谢稳态, 更可通过 DNA 甲基化修饰介导代际效应的传递, 显著增加子代肥胖、IR 以及脂质代谢紊乱的患病风险。值得强调的是, 母代运动干预作为一种多维度代谢调控手段, 不仅能够优化妊娠期母亲

的体重增长趋势, 缓解系统性炎症反应并降低妊娠并发症风险, 还能通过改善胎盘营养转运效率与分泌功能, 有效减轻母源性代谢应激对胎儿代谢系统的不良影响, 从而增强对子代糖脂代谢稳态的保护作用。重要的是, 母代营养与运动的交互作用可能通过协同或补偿的机制, 进一步放大这种代际健康效应。这种“营养-运动”动态平衡的调控模式, 为代际代谢疾病的精准预防和干预提供了新的思路。

尽管母代代谢健康对子代代谢易感性的研究已积累了大量成果, 但仍存在以下局限性, 亟待未来探索。a. 机制深度与跨代传递的争议。目前, 运动介导的“母亲-胎盘-胎儿”代谢交流网络尚未得到系统性阐明, 尤其是运动诱导的骨骼肌因子是否能够透过胎盘实现代际表观遗传信息传递, 仍需实验进一步验证。此外, 表观遗传标记的跨代稳定性及其与代谢表型的因果关联尚存争议, 需结合单细胞多组学技术与跨代动物模型深入探究。b. 性别特异性与生命周期效应。母代干预对子代代谢的影响存在显著性别差异, 但调控机制尚未明确。未来需整合性别特异性表观基因组、代谢组及微生物组数据, 解析雄性与雌性子代响应母代干预的分子分型。c. 营养-运动协同效应的动态阈值。营养与运动干预的协同效应可能受限于母体代谢弹性、干预时机及剂量。未来需构建“代谢弹性-干预剂量”动态模型, 结合实时代谢监测技术, 制定个性化干预方案。d. 临床转化与公共卫生策略。尽管动物实验揭示了母代干预的代际机制, 但人体研究仍面临伦理限制与长周期追踪的挑战。未来需开展多中心临床队列, 结合母婴生物样本库(如胎盘组织、脐血表观组)与人工智能预测模型, 筛选高危人群并验证干预策略的有效性。

因此, 未来的研究需要整合多组学技术与时空动态分析方法, 深入解析母亲-胎儿的代谢调控网络及“运动-营养”协同效应机制, 以期构建以发育源性机制为基础的代谢性疾病早期精准干预体系奠定坚实的理论基础。唯有通过跨学科协作、技术创新与政策支持, 方能将“生命早期健康促进”从理论推向实践, 为实现健康中国战略提供科学支撑。

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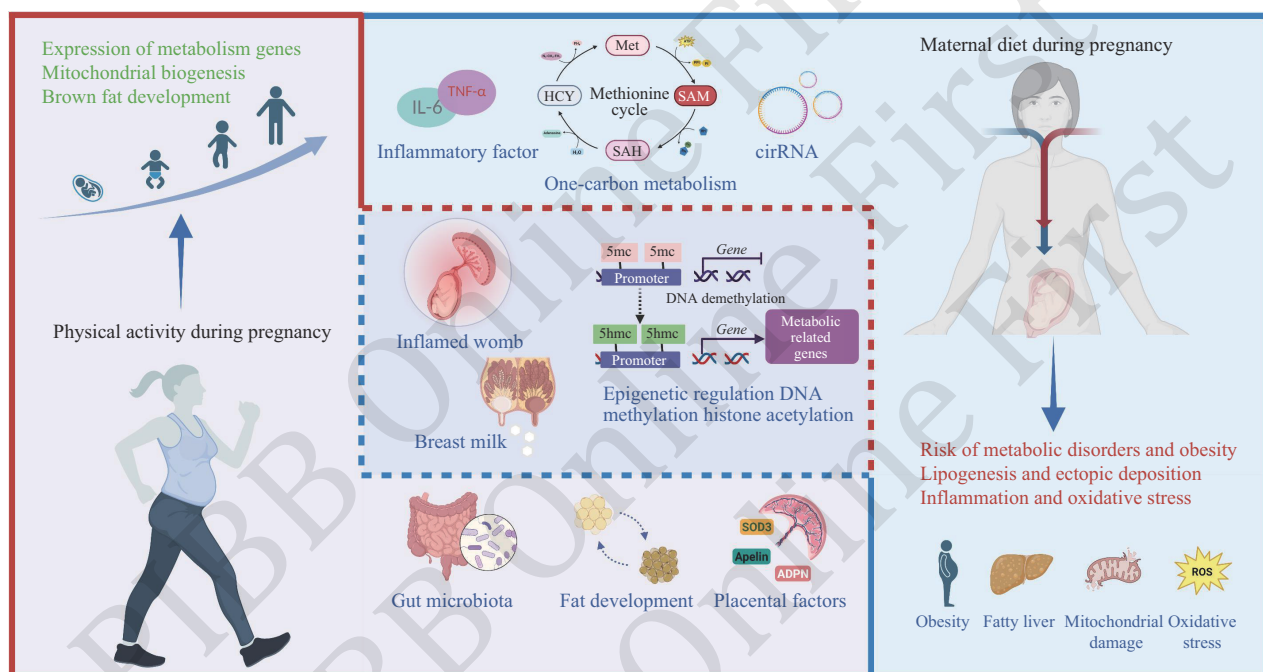
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Intergenerational Effects on Metabolic Health: Perspectives on Maternal Nutrition and Exercise During Pregnancy*

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Graphical abstract



Abstract With the increasing prevalence of overweight and obesity among children and adolescents in China, pediatric metabolic syndrome has emerged as a significant public health challenge. The Developmental Origins of Health and Disease (DOHaD) theory underscores the critical influence of early environmental factors on lifelong metabolic health. Consequently, maternal nutritional status and physical activity during pregnancy have become key modifiable factors that have attracted considerable attention in recent years. Research indicates exposure to a maternal high-fat diet (HFD) during pregnancy has long-term effects on offspring health, which may be transmitted through placental transit disorder, inflammation, and oxidative stress. Similarly, a high-protein diet (HPD) during pregnancy exhibits a dose- and time-dependent biphasic effect: excessive intake may lead to fetal growth restriction and an increased risk of preterm birth, whereas moderate supplementation may instead reduce

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the susceptibility of offspring to obesity. Interestingly, caloric restriction (CR) during pregnancy presents a double-edged sword: while it may impair the development of metabolic organs in offspring, moderate CR in metabolically compromised mothers can ameliorate maternal metabolic dysfunction and reprogram oocyte DNA methylation, significantly lowering the risk of metabolic disorders in offspring. Notably, metabolic abnormalities induced by a low-protein diet (LPD) during pregnancy demonstrate lifecycle-accumulative effects and transgenerational inheritance, with offspring exhibiting obesity phenotypes during weaning, insulin resistance in adulthood, and hepatic decompensation in old age, mediated through oocyte epigenetic reprogramming. Additionally, maintaining an optimal micronutrient balance is crucial for the metabolic homeostasis of offspring, as both deficiency and excess can lead to detrimental outcomes. Maternal exercise has been established as a safe and effective non-pharmacological intervention that confers multigenerational metabolic benefits through diverse biological pathways. Maternal metabolic dysregulation represents a critical determinant of offspring metabolic disorders. Regular exercise during gestation exerts protective effects by attenuating maternal systemic inflammation and reducing the incidence of pregnancy-related complications, thereby effectively mitigating fetal overgrowth and metabolic dysfunction. This dual benefit for both mother and offspring underscores the pivotal role of gestational physical activity in promoting long-term metabolic health. The placenta, serving as the exclusive interface for maternal-fetal communication, mediates exercise-induced metabolic programming through enhanced secretion of key regulatory factors (including SOD3, Apelin, ADPN, and Irisin) and promotes the development of vascular networks, collectively optimizing nutrient transport efficiency. The intrauterine period represents a crucial window for epigenetic reprogramming, during which maternal exercise modulates DNA methylation patterns of critical metabolic genes (*e. g.*, *Ppargc-1a*, *Prdm16*, *Klf4*, and *Slc23a2*) in offspring, thereby enhancing their capacity to resist metabolic disorders. Notably, the regulatory effects of maternal exercise extend beyond the gestational period. Postnatally, exercise-induced modifications in the bioactive components of breast milk and gut microbiota composition contribute to the sustained maintenance of metabolic homeostasis in offspring, establishing a continuum of metabolic protection from prenatal to postnatal stages. This review explores the potential of maternal combined nutrition-exercise interventions, suggesting that such strategies may synergistically enhance transgenerational health benefits through interactions within the metabolic-epigenetic network, thereby outperforming single interventions. Additionally, it examines current research limitations, including controversies surrounding transgenerational mechanisms, sex-specific responses, and undefined dynamic thresholds, while providing directions for future investigations. These findings pave the way for a theoretical foundation for early-life health interventions, potentially offering a more effective strategy for combatting intergenerational metabolic disorders.

Key words nutrition during pregnancy, maternal exercise, epigenetic regulation, metabolic programming, intergenerational effects

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