网络出版时间:2025 - 02 - 06 14:15:40 网络出版地址:https://link.cnki.net/urlid/34.1065.R.20250206.1140.026

产前应激通过破坏子代肠道菌群导致疾病的研究进展

何鉴芝*,曾词正*,陈雪梅,谢谕威,敖 当,刘 玲 综述 李 文 审校
(广东医科大学附属医院儿科,湛江 524001)

摘要 产前应激(PS)是母体妊娠时一种常见的全身性、非特异性应激反应。肠道菌群被称为人体的第二基因组,与人体各大系统相互作用。肠道菌群的改变会影响婴幼儿的发育和健康。随着研究技术的发展,逐渐揭示 PS 与子代肠道菌群失衡及多个系统疾病的关系。然而,PS 破坏子代肠道微生物群的确切机制尚未完全清楚。该文通过对 PS 破坏子代肠道菌群导致疾病的现有研究进行总结,寻找未来的研究方向,以拓展对婴幼儿疾病发病机制的认知。

关键词 产前应激;母体;肠道菌群;失调;子代;疾病
中图分类号 R 725
文献标志码 A **文章编号** 1000 - 1492(2025)02 - 0372 - 06
doi:10.19405/j.cnki.issn1000 - 1492.2025.02.027

产前应激(prenatal stress, PS)作为一种生命早期的影响因素,对母体本身和子代都有着不利的深远影响[1]。据统计约 75% 的孕妇经历过 PS[2-3],10% ~35% 的儿童受到母亲抑郁的影响[4],PS 对个人、家庭、社会均产生巨大的经济负担。近年来研究[5-6]证实肠道微生物群在 PS 与子代疾病的关系中发挥了重要作用。因此,该文对 PS 通过影响子代肠道菌群而导致疾病的研究现状进行回顾(图 1),并对某些疾病的菌群特征和标志物进行归纳,为婴幼儿疾病的早期诊断与治疗提供新的思路。

1 PS 与子代肠道菌群

PS 是孕期母体受到内外环境变化及精神心理因素等刺激时发生的适应性应激反应[7]。妊娠是一个生理和心理长期变化的过程,在这个过程中母体面临着社会因素、个人心理因素、家庭因素、灾难暴露等一系列衍生应激源的影响[8-9]。现已证实 PS 会导致子代生长发育障碍、免疫功能紊乱和疾病易感性增加等[9-10]。生命早期是肠道菌群形成的关键时期,受到孕产妇饮食、抗生素使用、分娩方式、母乳喂养、孕产妇压力、环境和疾病等多种因素的影响[11-13]。肠道菌群参与了食物消化、营养吸收和代谢产物合成等过程,在人体发育、代谢、免疫和心理方面发挥着重要的作用[14]。研究[6,11,15]发现,PS 改变了母体胃肠道和阴道微生物群的组成,再垂直传递给子代,从而导致子代肠道微生物的失调。PS 中的母体还会产生过高的皮质醇,皮质醇会通过胎盘和母乳传递给胎儿而影响胎儿的肠道微生物[16-17]。此外,PS 可能通过诱导胎儿肠道中与炎症和免疫细胞募集相关的基因(如 Slamf7, Defa-rs7, Raet1e, Ceacam2, C2, MyD88, Irak1, Traf6, TNF-α 等)表达而导致子代的肠道菌群生态失调[6,18]。婴幼儿肠道菌群的失调影响其多个系统的发育与健康[12]。因此探索子代肠道菌群失调与疾病的关系和维持生态系统的平衡显得尤为重要。

2 PS 破坏子代肠道菌群与疾病的关系

PS 可通过影响子代菌群的定植、激素水平和基因表达等途径来破坏子代肠道菌群的平衡,并由此介导子代神经、免疫、消化和呼吸系统相关疾病的发生发展(图 2)。

2.1 PS 引发子代肠道微生物组变化与神经系统疾病之间的关联 PS 与子代菌群的定植和神经系统疾病之间存在一定的关系,已有一些研究[5,19]表明早期生活经历(包括孕期经历的应激)会对婴儿的肠道菌群形成和神经系统的发育产生影响。国内一项前瞻性纵向研究[20]发现,PS 通过改变生命早期肠道微生物的建立来影响婴幼儿长期的行为气质和情绪反应,尤其强调了 PS 通过增加子代肠道伯克霍

2024 - 09 - 29 接收
基金项目:广东医科大学附属医院高层次人才科研启动项目(编号:GCC2021009)
作者简介:何鉴芝,女,硕士研究生;
李 文,女,助理研究员,硕士生导师,通信作者,E-mail:liwen410@163.com
* 对本文具有同等贡献

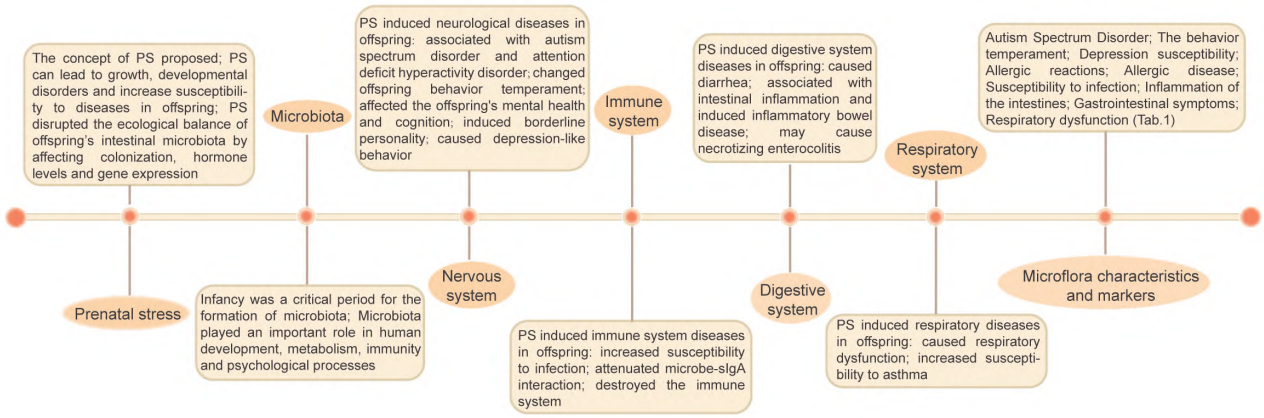

图 1　PS 概念的提出及其与子代肠道菌群和疾病关系的研究进展示意图

Fig. 1　Research progress on the concept of PS and its relationship with intestinal microbiota and diseases in offspring

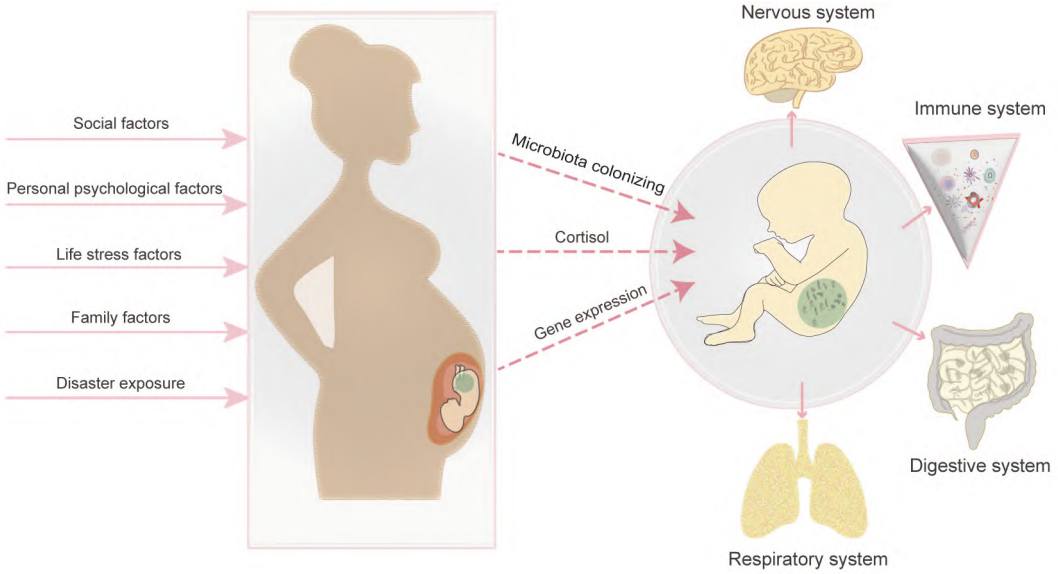

图 2　PS 通过破坏子代肠道菌群导致疾病

Fig. 2　PS induced disease by disrupting offspring's intestinal microbiota

尔德菌的丰富度调控子代肠道行为。与其相似的是美国一项纵向研究[19]发现,非裔美国婴儿大脑发育迟缓与 PS 破坏婴儿微生物的组成相关。早期生活压力和婴幼儿肠道微生物群对婴幼儿心理健康和神经认知发展有一定影响,但在发育早期恢复肠道菌群可以逆转 PS 对子代认知的影响[21]。在边缘型人格障碍的病理研究中认为母亲产前压力导致婴幼儿肠道微生物失衡,进而影响杏仁核的发育以及杏仁核与其他大脑区域的相互作用[22]。此外,PS 导致子代肠道微生物群失调进而影响婴幼儿代谢途径来促进 PS 诱导的抑郁样行为的发生[23]。另有学者提出 PS 还可能与子代自闭症谱系障碍和注意缺陷多动障碍之间存在关系[24]。由此可见,PS 会通过破坏子代肠道菌群而导致子代神经系统的发育障碍。然而,肠道菌群在 PS 和子代神经系统疾病中的作用机制尚不完全清楚。目前认为 PS 通过影响子代微生物群—肠—脑轴、免疫因子、下丘脑—垂体—肾上腺轴和胎儿的表观遗传学调节等诱导神经系统的发育和功能障碍[25-28]。姚余有教授研究团队还发现 PS 导致子代抑郁样行为具有性别差异,子代雄鼠的抑郁样行为较雌鼠更为明显[29],提示肠道菌群在子代疾病的作用机制或可是未来研究的方向之一。

2.2 PS 改变子代肠道菌群在免疫系统疾病中的潜在作用 胎儿的免疫系统在孕期逐渐发育,而肠道微生物群被认为是 PS 影响母体和子代免疫功能的潜在机制[30]。母亲的抑郁症状和应激症状轨迹与婴儿粪便的分泌性免疫球蛋白 A(secretory immunoglobulin A, sIgA)浓度之间存在关联,母体妊娠时的应激反应会降低微生物与 sIgA 间的相互作用,增加子代难辨梭菌的定植和过敏性疾病发生的风险[31-32]。还有研究[30]发现 PS 会导致母体和子代的免疫功能障碍,且母体压力和肠道微生物在影响母体和子代免疫功能方面的作用相似但离散。此外,PS 会降低子代双歧杆菌属和乳酸杆菌属的细菌丰度及增加子代最初 6 个月的感染率[33]。

PS 会改变母体和子代的肠道菌群,而肠道菌群的失调与免疫系统的调节密切相关。实验动物模型显示,暴露于母体压力,会破坏母体和子代肠道菌群和免疫系统的发育,增加子代患上免疫系统疾病的风险,但目前对人类的研究还很少[30-32]。

2.3 PS 导致子代肠道菌群失衡对消化系统的影响 PS 会导致子代肠道微生物的多样性与丰度的改变、胃肠道的免疫和功能障碍、结肠的神经支配减少等,这些影响都可能增加子代患上消化系统疾病的风险[34-35]。孕期经历 PS 与未经历的恒河猴子代相比,双歧杆菌和乳酸杆菌的水平更低,腹泻症状更多[36]。与此研究一致的是经历反复约束应激的小鼠子代肠道菌群有益菌减少且促炎菌增加,表明 PS 增加了子代小鼠肠道炎症的易感性,并且 PS 可能通过微生物群—肠—脑轴和神经内分泌系统失调来促进炎症性肠病(如克罗恩病和溃疡性结肠炎)的发生[37]。此外,PS 会改变子代变形菌门的相对丰度,而 γ-变形菌与人类婴儿坏死性小肠结肠炎有关[15]。

这些报道阐明了 PS 导致子代肠道菌群失调而增加消化系统疾病风险的原因,但目前对于 PS 通过影响子代肠道菌群而导致的消化系统疾病的研究还寥寥无几。因此,尽管有一些证据表明 PS 与消化系统疾病的发病风险相关,仍需要探索更多的研究证据。

2.4 PS 对子代肠道菌群的破坏与呼吸系统疾病的可能联系 一项队列研究[38]显示,母体焦虑抑郁和负面生活事件与子代哮喘的发生有关。此外,在妊娠期间暴露于压力或精神健康问题的子代患哮喘疾病的风险增加[39-41]。虽然目前尚无研究明确表明肠道菌群失衡在 PS 与子代呼吸系统疾病中的重要作用,但在慢性 PS 的大鼠模型研究中发现,子代某些肠道细菌的丰度与呼吸功能障碍呈正相关;并且 PS 诱导子代胃肠道和呼吸系统长期适应不良,且伴有肠道微生物组的改变[34]。婴儿胃肠菌群中的脉原体与慢性肺病相关,鉴于 PS 与子代肠道菌群失调的高度相关性及肠道菌群与呼吸系统的相互联系,不难得出 PS 导致子代呼吸系统疾病的重要机制之一可能是通过破坏子代的肠道菌群[6, 36, 42]。总之,早期生活的不良事件会增加子代患呼吸系统疾病的风险。PS 对子代的呼吸系统产生一定影响,尤其是在哮喘的发病风险和呼吸功能方面。近年来学者提出的肺—肠轴的概念可以解释他们的关系,即肠道微生物群的组成和功能变化可以影响肺部的健康[43]。

3 PS 导致子代疾病的肠道菌群特征和生物标志物

生物标志物是指在生物体内可以测量或检测的特定分子、细胞或生物体的生理状态,其对于疾病的早期诊断、疾病进展的监测、治疗效果评估等方面具有重要的临床应用价值[44]。PS 会破坏子代肠道菌群,而一些菌群特征和标志物与某些疾病有着密切的联系,本文总结了现研究中与 PS 相关的子代疾病的肠道菌群特征和标志物,具体见表 1。

4 总结与展望

PS 作为生命早期的影响因素之一,通过多种途径破坏子代肠道菌群,进而影响子代的发育与健康。合理干预母体和子代肠道菌群的平衡和激素水平有望预防 PS 导致的子代疾病。肠道菌群与疾病的关系及微生物与宿主的相互作用是目前研究的热点之一,然而,对 PS 破坏子代肠道菌群导致疾病的机制研究以及生物标志物和预测却鲜有报道。此外,考虑到 PS 与子代后续环境因素(例如社会支持、医疗服务和饮食干预等)的复杂互动关系,后续还需要开展更长时间的纵向队列研究来追踪 PS 对子代健康的长期影响,并探索有效的预防和干预策略,以改善儿童的健康状况。

表1 PS导致子代疾病的肠道菌群特征及生物标志物

Tab.1 Characteristics of intestinal microbiota and biomarkersof diseases in offspring caused by PS

Disease	Microflora characteristics	Markers	Reference
Autism Spectrum Disorder	The abundance of Proteobacteria increased; The abundance of *Alcaligenaceae*, *Enhydrobacter*, *Chryseobacterium*, *Streptococcus*, *Acinetobacter*, *Wautersiella*, *Agrobacterium*, *Parabacteroides* and *Acinetobacterjohnsonii* increased significantly; The abundance of *Prevotella* reduced; There was no significant difference in the diversity of intestinal microbiota.	*Betaproteobacteria*, *Burkholderiales*, *Pseudomonadales*, *Moraxellaceae and Acinetobacter*	[45]
Behavior temperament	The relative abundance of *Burkholderia* reduced; The relative abundance of *Bifidobacterium* increased.	*Burkholderia*	[20]
Depression susceptibility	Alpha diversity and Beta diversity were changed by PS; The most abundant microbiota of mouse offspring under PS was *Lactobacillus*, *S24-7-unclassified*, *Kurthia*, *Weissell*, *Corynebacterium* and incertai-sedis.	–	[23]
Allergic reactions	The relative abundance of contain pathogens (related to *Escherichia*, *Serratia*, and *Enterobacter*) increased; The relative abundance of lactic acid bacteria (i.e., *Lactobacillus*, *Lactoccus*, *Aerococcus*) and *Bifidobacteria* reduced.	–	[33]
Allergic disease	The association of *Bacteriodes* genus and *Escherichia* species with sIgA decreased.	sIgA decreased	[31]
Susceptibility to infection	The profile of total aerobes and facultative anaerobes was biphasic, with peak concentrations occurring between 2 and 16 weeks of age; The numbers of *Bifidobacteria* and *Lactobacilli* were low at 2 days after birth but rapidly increased to a peak between 8 and 16 weeks of age.	–	[36, 46]
Inflammation of the intestines	The abundance of *Desulfovibrionales*, *Desulfovibrionaceae*, *Desulfovibrio* and Gram-positive coccus pathogens (such as *Streptococcus* and *Enterococcus*) increased; The abundance of *Bifidobacteriales*, *Bifidobacteriaceae*, *Bifidobacterium* and short-chain fatty acid (SCFA)-producing bacteria (such as *Blautia and Robinsoniella*) reduced.	Desulfovibrionales, Desulfovibrionaceae and Desulfovibrio were persisting; Desulfovibrio was positively correlated with intestinal inflammatory factors	[37]
Gastrointestinal symptoms	The abundance of lactic acid bacteria and *Bifidobacteria* reduced.	–	[33]
Respiratory dysfunction	The abundance of *Papillibacter* increased.	–	[34]

参考文献

[1] Huot R L, Brennan P A, Stowe Z N, et al. Negative affect in offspring of depressed mothers is predicted by infant cortisol levels at 6 months and maternal depression during pregnancy, but not postpartum[J]. Ann N Y Acad Sci, 2009, 1032(1): 234-6. doi: 10.1196/annals.1314.028.

[2] Schetter D C. Psychological science on pregnancy: stress processes, biopsychosocial models, and emerging research issues[J]. Annu Rev Psychol, 2011, 62: 531-58. doi:10.1146/annurev.psych.031809.130727.

[3] Woods S M, Melville J L, Guo Y, et al. Psychosocial stress during pregnancy[J]. Am J Obstet Gynecol, 2010, 202(1): 61.e1-7. doi:10.1016/j.ajog.2009.07.041.

[4] Maselko J, Sikander S, Bhalotra S, et al. Effect of an early perinatal depression intervention on long-term child development outcomes: follow-up of the thinking healthy programme randomised controlled trial[J]. Lancet Psychiatry, 2015, 2(7): 609-17. doi:10.1016/S2215-0366(15)00109-1.

[5] Jasarevic E, Howerton C L, Howard C D, et al. Alterations in the vaginal microbiome by maternal stress are associated with metabolic reprogramming of the offspring gut and brain[J]. Endocrinology, 2015, 156(9): 3265-76. doi:10.1210/en.2015-1177.

[6] Yeramilli V, Cheddadi R, Shah J, et al. A review of the impact of maternal prenatal stress on offspring microbiota and metabolites [J]. Metabolites, 2023, 13(4): 535. doi: 10.3390/metabo13040535.

[7] Keeley K. Prenatal influence on behavior of offspring of crowded mice[J]. Science, 1962, 135(3497): 44-5. doi:10.1126/science.135.3497.44.

[8] Saur A M, Dos Santos M A. Risk factors associated with stress symptoms during pregnancy and postpartum: Integrative literature review[J]. Women Health, 2021, 61(7): 651-67. doi:10.1080/03630242.2021.1954132.

[9] Van Den Bergh B R H, Van Den Heuvel M I, Lahti M, et al. Prenatal developmental origins of behavior and mental health: the influence of maternal stress in pregnancy[J]. Neurosci Biobehav Rev, 2020, 117: 26-64. doi:10.1016/j.neubiorev.2017.07.003.

[10] Naudé P J W, Claassen-Weitz S, Gardner-Lubbe S, et al. Associ-

ation of maternal prenatal psychological stressors and distress with maternal and early infant faecal bacterial profile[J]. Acta Neuropsychiatr, 2020, 32(1): 32 – 42. doi:10.1017/neu.2019.43.

[11] Wang S, Ryan C A, Boyaval P, et al. Maternal vertical transmission affecting early-life microbiota development[J]. Trends Microbiol, 2020, 28(1): 28 – 45. doi:10.1016/j.tim.2019.07.010.

[12] Ronan V, Yeasin R, Claud E C. Childhood development and the microbiome-the intestinal microbiota in maintenance of health and development of disease during childhood development[J]. Gastroenterology, 2021, 160(2): 495 – 506. doi:10.1053/j.gastro.2020.08.065.

[13] Wang S, Egan M, Ryan C A, et al. A good start in life is important-perinatal factors dictate early microbiota development and longer term maturation[J]. FEMS Microbiol Rev, 2020, 44(6): 763 – 81. doi:10.1093/femsre/fuaa030.

[14] Loniewska B, Loniewski I. Effect of pre- and perinatal factors and infant nutrition on the intestinal microbiota[J]. Nutrients, 2023, 15(18): 3977. doi:10.3390/nu15183977.

[15] Agusti A, Lamers F, Tamayo M, et al. The gut microbiome in early life stress: a systematic review[J]. Nutrients, 2023, 15(11): 2566. doi:10.3390/nu15112566.

[16] Hechler C, Borewicz K, Beijers R, et al. Association between psychosocial stress and fecal microbiota in pregnant women[J]. Sci Rep, 2019, 9(1): 4463. doi:10.1038/s41598 – 019 – 40434 – 8.

[17] Zijlmans M A, Riksen-Walraven J M, De Weerth C. Associations between maternal prenatal cortisol concentrations and child outcomes: a systematic review[J]. Neurosci Biobehav Rev, 2015, 53: 1 – 24. doi:10.1016/j.neubiorev.2015.02.015.

[18] Jasarevic E, Howard C D, Morrison K, et al. The maternal vaginal microbiome partially mediates the effects of prenatal stress on offspring gut and hypothalamus[J]. Nat Neurosci, 2018, 21(8): 1061 – 71. doi:10.1038/s41593 – 018 – 0182 – 5.

[19] Brennan P A, Dunlop A L, Smith A K, et al. Protocol for the emory university african american maternal stress and infant gut microbiome cohort study[J]. BMC Pediatr, 2019, 19(1): 246. doi:10.1186/s12887 – 019 – 1630 – 4.

[20] Zhang X, Huang Y, Lu Y, et al. Associations of maternal antenatal bonding with neonatal meconium microbiota and the behavior temperament of infants: a prospective longitudinal study[J]. J Psychiatr Res, 2023, 163: 159 – 65. doi:10.1016/j.jpsychires.2023.05.053.

[21] Vogel S C, Brito N H, Callaghan B L. Early life stress and the development of the infant gut microbiota: implications for mental health and neurocognitive development[J]. Curr Psychiatry Rep, 2020, 22(11): 61. doi:10.1007/s11920 – 020 – 01186 – 9.

[22] Anderson G. Pathoetiology and pathophysiology of borderline personality: role of prenatal factors, gut microbiome, mu- and kappa-opioid receptors in amygdala-PFC interactions[J]. Prog Neuropsychopharmacol Biol Psychiatry, 2020, 98: 109782. doi:10.1016/j.pnpbp.2019.109782.

[23] Li Q, Sun H, Guo J, et al. The effect of prenatal stress on offspring depression susceptibility in relation to the gut microbiome and metabolome[J]. J Affect Disord, 2023, 339: 531 – 7. doi:10.1016/j.jad.2023.07.089.

[24] Manzari N, Matvienko-Sikar K, Baldoni F, et al. Prenatal maternal stress and risk of neurodevelopmental disorders in the offspring: a systematic review and meta-analysis[J]. Soc Psychiatry Psychiatr Epidemiol, 2019, 54(11): 1299 – 309. doi:10.1007/s00127 – 019 – 01745 – 3.

[25] Van Den Bergh B R H, Dahnke R, Mennes M. Prenatal stress and the developing brain: risks for neurodevelopmental disorders[J]. Dev Psychopathol, 2018, 30(3): 743 – 62. doi:10.1017/s0954579418000342.

[26] Frankiensztajn L M, Elliott E, Koren O. The microbiota and the hypothalamus-pituitary-adrenocortical (HPA) axis, implications for anxiety and stress disorders[J]. Curr Opin Neurobiol, 2020, 62: 76 – 82. doi:10.1016/j.conb.2019.12.003.

[27] Rotem-Kohavi N, Keane J, Clarke G, et al. The microbiome-gut-brain axis: a new window to view the impact of prenatal stress on early neurodevelopment[M]//Ashley Wazana. Prenatal Stress and Child Development. Cham: Springer International Publishing, 2021: 165 – 91. doi:10.1007/978 – 3 – 030 – 60159 – 1_8.

[28] Laue H E, Karagas M R, Coker M O, et al. Sex-specific relationships of the infant microbiome and early-childhood behavioral outcomes[J]. Pediatr Res, 2022, 92(2): 580 – 91. doi:10.1038/s41390 – 021 – 01785 – z.

[29] 刘 锐, 屠心茹, 陶 龙, 等. 妊娠期慢性应激致子代小鼠杏仁核神经元损伤和抑郁样行为[J]. 安徽医科大学学报, 2022, 57(12): 1947 – 53. doi:10.19405/j.cnki.issn1000 – 1492.2022.12.017.

[29] Liu R, Tu X R, Tao L, et al. Neuron injury of amygdala and depression – like behavior in offspring mice induced by chronic pregnancy stress[J]. Acta Univ Med Anhui, 2022, 57(12): 1947 – 53. doi:10.19405/j.cnki.issn1000 – 1492.2022.12.017.

[30] Chen H J, Bischoff A, Galley J D, et al. Discrete role for maternal stress and gut microbes in shaping maternal and offspring immunity[J]. Neurobiol Stress, 2022, 21: 100480. doi:10.1016/j.ynstr.2022.100480.

[31] Kang L J, Koleva P T, Field C J, et al. Maternal depressive symptoms linked to reduced fecal immunoglobulin a concentrations in infants[J]. Brain Behav Immun, 2018, 68: 123 – 31. doi:10.1016/j.bbi.2017.10.007.

[32] Kang L J, Vu K N, Koleva P T, et al. Maternal psychological distress before birth influences gut immunity in mid-infancy[J]. Clin Exp Allergy, 2020, 50(2): 178 – 88. doi:10.1111/cea.13551.

[33] Zijlmans M A, Korpela K, Riksen-Walraven J M, et al. Maternal prenatal stress is associated with the infant intestinal microbiota[J]. Psychoneuroendocrinology, 2015, 53: 233 – 45. doi:10.1016/j.psyneuen.2015.01.006.

[34] Golubeva A V, Crampton S, Desbonnet L, et al. Prenatal stress-induced alterations in major physiological systems correlate with gut microbiota composition in adulthood[J]. Psychoneuroendocrinology, 2015, 60: 58 – 74. doi:10.1016/j.psyneuen.2015.06.

002.

[35] Rusconi F, Gagliardi L, Gori E, et al. Perinatal maternal mental health is associated with both infections and wheezing in early childhood[J]. Pediatr Allergy Immunol, 2019, 30(7): 732-8. doi:10.1111/pai.13103.

[36] Fanaroff A A. Prenatal stress alters bacterial colonization of the gut in infant monkeys[J]. Yearb Neonatal Perinat Med, 2006, 2006: 82-3. doi:10.1016/s8756-5005(08)70246-4.

[37] Sun Y, Xie R, Li L, et al. Prenatal maternal stress exacerbates experimental colitis of offspring in adulthood[J]. Front Immunol, 2021, 12: 700995. doi:10.3389/fimmu.2021.700995.

[38] Magnus M C, Wright R J, Røysamb E, et al. Association of maternal psychosocial stress with increased risk of asthma development in offspring[J]. Am J Epidemiol, 2018, 187(6): 1199-209. doi:10.1093/aje/kwx366.

[39] Cookson H, Granell R, Joinson C, et al. Mothers' anxiety during pregnancy is associated with asthma in their children[J]. J Allergy Clin Immunol, 2009, 123(4): 847-53. e11. doi:10.1016/j.jaci.2009.01.042.

[40] De Marco R, Pesce G, Girardi P, et al. Foetal exposure to maternal stressful events increases the risk of having asthma and atopic diseases in childhood[J]. Pediatr Allergy Immunol, 2012, 23(8): 724-9. doi:10.1111/j.1399-3038.2012.01346.x.

[41] Liu X, Madsen K P, Sejbaek C S, et al. Risk of childhood asthma following prenatal exposure to negative life events and job stressors: a nationwide register-based study in denmark[J]. Scand J Work Environ Health, 2019, 45(2): 174-82. doi:10.5271/sjweh.3785.

[42] Loverdos K, Bellos G, Kokolatou L, et al. Lung microbiome in asthma: current perspectives[J]. J Clin Med, 2019, 8(11): 1967. doi:10.3390/jcm8111967.

[43] Samuelson D R, Welsh D A, Shellito J E. Regulation of lung immunity and host defense by the intestinal microbiota[J]. Front Microbiol, 2015, 6: 1085. doi:10.3389/fmicb.2015.01085.

[44] Ilyin S E, Belkowski S M, Plata-Salamán C R. Biomarker discovery and validation: technologies and integrative approaches[J]. Trends Biotechnol, 2004, 22(8): 411-6. doi:10.1016/j.tibtech.2004.06.005.

[45] 李 宁. 孤独症谱系障碍儿童母子肠道菌群相关性及潜在风险评估标志物研究[D]. 济南: 山东大学, 2019.

[45] Li N. Correlation of gut microbiome between ASD children and mothers and potential biomarkers for risk assessment[D]. Jinan: Shandong University, 2019.

[46] Bailey M T, Lubach G R, Coe C L. Prenatal stress alters bacterial colonization of the gut in infant monkeys[J]. J Pediatr Gastroenterol Nutr, 2004, 38(4): 414-21. doi:10.1097/00005176-200404000-00009.

Recent research progress of prenatal stress-induced disease by disrupting offspring intestinal microbiota

He Yingzhi, Zeng Cizheng, Chen Xuemei, Xie Yuwei, Ao Dang, Liu Ling, Li Wen

(*Dept of Pediatrics, The Affiliated Hospital of Guangdong Medical University, Zhanjiang* 524001)

Abstract Prenatal stress is a common, systemic, nonspecific stress response that occurs during pregnancy. The gut microbiota, which is known as the "second genome" of the human body, interacts with all major systems of the body. Changes in the gut microbiota can impact the development and health of infants and young children. Advances in research technology have allowed us to uncover the relationship between prenatal stress and imbalances in offspring intestinal microbiota, as well as the development of multiple systemic diseases. However, the exact mechanisms through which prenatal stress disrupts the gut microbiota of offspring remain incompletely understood. This review summarizes the existing research on diseases caused by prenatal stress disrupting the offspring intestinal flora, and seeks future research directions to expand the understanding of the pathogenesis of infant diseases.

Key words prenatal stress; parent; microbiota; imbalance; offspring; disease

Fund program High-Level Talents Scientific Research Start-Up Foundation of The Affiliated Hospital of Guangdong Medical University (No. GCC2021009)

Corresponding author Li Wen, E-mail: liwen410@163.com