· 综述 ·

微塑料对动物神经发育和行为学的影响及其机制研究

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【摘要】 微塑料（直径＜5 mm的塑料颗粒）作为一类新型环境污染物，已在多种环境介质及食品中被检出。已有研究表明，微塑料可透过血脑屏障作用于动物中枢神经系统，其作用效应及分子机制亟待阐明。现系统综述微塑料暴露对动物的神经系统发育、认知与学习、情绪及行为的影响，并探讨了其潜在作用机制，包括氧化应激、神经炎症及神经递质失调，以期进一步揭示微塑料的神经毒性作用，提供潜在分子干预途径。

【关键词】 微塑料； 神经发育； 行为学； 综述
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Impact of microplastics on animal neurodevelopment and behavior and its mechanisms *Qiu Yedan*, *Liu Qianqi*
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【**Abstract**】 Microplastics (plastic particles ＜ 5 mm in diameter), as a new class of environmental contaminants, have been detected in a variety of environmental media and food products. It has been shown that microplastics can cross the blood-cerebrospinal fluid barrier and act on the central nervous system of animals, and their effects and molecular mechanisms need to be elucidated. This paper systematically reviews the impact of microplastic exposure on neurological development, cognition and learning, emotion and behavior in animals, and explores the potential mechanisms of action, including oxidative stress, neuroinflammation and neurotransmitter dysregulation, with a view to further revealing the neurotoxic effects of microplastics and providing potential molecular intervention pathways.

【**Key words**】 Microplastics； Neurodevelopment； Behavioral sciences； Review
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微塑料是指粒径＜5 mm的塑料颗粒，其中直径＜1 μm的塑料颗粒则被称为纳米塑料[1]。微塑料具有广泛的环境分布特征，已在各类生态系统中被检测到[2]，包括南极等偏远区域[3]，其环境浓度随塑料使用量增加而显著升高[4]。微塑料污染已成为全球性环境问题[5]。现有研究证实，动物可通过多种途径摄入微塑料，进而对多个生理系统造成不良影响，涉及消化、呼吸、神经、免疫和生殖功能等[6]。研究表明，微塑料可突破血脑屏障，沉积在脑组织中[7]，提示其可能干扰神经系统功能。虽然目前关于微塑料毒理学效应的研究已取得一些成果，但其如何影响神经系统及具体分子机制仍需进一步探究。本文综述了微塑料对动物神经发育和行为学的具体影响及其分子机制研究进展，旨在揭示微塑料暴露与神经精神疾病之间的作用关系，并提供潜在的分子干预途径。

一、微塑料对动物神经发育和行为学的影响

1.对动物神经系统发育的影响：现有证据表明，微塑料可通过多种途径对鱼类和啮齿类动物的神经系统发育造成损害，其毒性效应具有显著的跨代传递特征。Zhou等[8]对转基因斑马鱼的实验发现，不同粒径（100、500、1 000 nm）的聚苯乙烯纳米塑料（polystyrene nanoplastics，PS-NPs）暴露均会引发胚胎神经毒性，导致子代神经元损伤、轴突发育异常及相关基因表达改变，最终产生行为异常。Jeong等[9]的研究显示，当妊娠期和哺乳期母鼠经口摄入PS-NPs

时，子代小鼠海马区与神经干细胞增殖相关基因的转录表达水平下降，神经胶质细胞能量代谢失衡，CA3区神经元层厚度及胼胝体体积显著减小。此外，高浓度微塑料暴露组中的雌性子代还表现出特有的神经功能障碍和认知能力缺陷。另一项对小鼠的研究显示，亲代小鼠口服微塑料和纳米塑料后可诱发子代大脑氧化损伤，并减少脑中GABA的合成，进而导致子代焦虑样行为[10]。纳米塑料被孕期大鼠摄入后，可以通过并破坏胎盘屏障，诱发子代部分脑区(前额叶皮质、海马及纹状体)的氧化应激及炎性反应，进而对子代小鼠产生神经发育毒性[11]。这些发现系统阐明了微塑料通过直接发育毒性和跨代遗传调控损害神经系统的发育，为评估其神经发育风险提供了关键证据。

2.对动物认知和学习能力的影响：微塑料的暴露可导致动物认知和记忆缺陷[12]。Lee等[13]通过8周聚苯乙烯微塑料(polystyrene microplastics，PS-MPs)暴露模型发现，小鼠海马区出现α-氨基-3-羟基-5-甲基-4-异恶唑丙酸受体(α-amino- 3-hydroxy-5-methyl-4-isoxazole-propionic acid receptor，AMPAR)异常激活、即刻早期基因表达抑制及神经炎性级联反应，这些分子病理特征共同导致突触可塑性受损和记忆功能障碍。值得注意的是，不同脑区对微塑料暴露具有差异敏感性。Chu等[14]研究证实长期PS-MPs暴露可特异性损伤前额叶皮层，诱导剂量依赖性认知衰退，表现为空间学习与记忆保留能力随暴露剂量升高呈梯度下降。Yang等[15]进一步发现未成年个体对聚丙烯微塑料暴露更为敏感，其神经认知缺陷程度与暴露剂量呈显著正相关。研究表明，微塑料还可发挥化学载体效应增强神经毒性。研究显示，微塑料与增塑剂邻苯二甲酸二(2-乙基己基)酯(di-2-ethylhexyl phthalate，DEHP)联合暴露时，通过促进DEHP在脑组织的生物蓄积可产生显著的协同毒性作用。相较于单一暴露组，联合暴露组小鼠的认知记忆功能损伤程度加剧[16]。以上研究表明，微塑料暴露可通过多种病理机制导致动物认知和学习功能损伤。

3.对动物情绪和行为模式的影响：微塑料暴露可改变动物的情绪和行为模式。实验研究表明，斑马鱼暴露于微塑料后，其游泳速率与活动范围呈现剂量依赖性下降，并伴随浅滩行为、焦虑样反应及环境回避行为等异常行为表现[17]。哺乳动物模型中，微塑料暴露可诱发特征性行为学改变。旷场实验显示，暴露组小鼠呈现运动距离缩短及速度减缓等焦虑样行为特征[18]；纳米塑料暴露则进一步导致小鼠出现焦虑[19]、抑郁样行为及社交能力缺陷等多维度行为障碍[20]。更有意义的是，微塑料的神经行为毒性具有跨代际传递特性，即孕期PS-MPs暴露可诱导母源性微塑料经胎盘迁移至子代脑组织，引发子代小鼠焦虑、抑郁样行为及社交功能障碍[21]。Zaheer等[22]通过建立孕期聚乙烯微塑料暴露模型发现，子代小鼠表现出显著的孤独症谱系障碍样行为特征，具体表现为社交互动频率与自发交替行为减少，对新环境的探索欲望明显减弱，呈现出重复和强迫性的行为模式。以上研究结果提示微塑料可能通过干扰神经发育程序诱导异常行为模式。

二、微塑料对动物神经系统的毒性作用机制

1.氧化应激：氧化应激指的是体内氧化与抗氧化系统失衡的一种病理状态，其核心作用机制涉及活性氧的动态平衡失调，生理状态下，活性氧的产生与代谢对维持正常细胞功能具有重要作用，但在中枢神经系统中，过量活性氧可导致神经细胞核酸、蛋白质及脂质发生氧化损伤，进而引发神经功能障碍[23]。目前研究表明，微塑料的神经毒性效应与其调控活性氧生成及核转录因子红系2相关因子2(nuclear factor-erythroid 2-related factor 2，Nrf2)信号通路密切相关[24]。多项实验模型证实微塑料暴露可诱发特征性氧化应激反应。在鳜鱼模型中，Chen等[25]发现微塑料不仅抑制神经系统相关基因表达，还通过降低抗氧化酶活性破坏血脑屏障完整性。青鳉鱼暴露于PS-MPs的研究显示，随暴露浓度升高，脑组织过氧化氢酶和超氧化物歧化酶(superoxide dismutase，SOD)活性呈剂量依赖性降低，同时伴随丙二醛含量显著升高及脑水肿病理改变[26]。斑马鱼实验进一步揭示，纳米塑料可通过激活p38 丝裂原活化蛋白激酶(p38 Mitogen-Activated Protein Kinase, p38-MAPK)信号通路诱导氧化应激相关神经细胞凋亡[27]。在啮齿动物模型中也观察到了类似的结果。Wang等[28]发现，微塑料暴露组小鼠脑组织中的活性氧和丙二醛水平增加，谷胱甘肽水平降低，而抗氧化剂维生素E干预可逆转其学习记忆损伤。值得注意的是，PS-NPs暴露可激活大鼠海马组织氧化应激系统，具体表现为过氧化物酶(peroxidase，POD)及谷胱甘肽S-转移酶(glutathione S-transferase，GST)的活性显著升高，进而导致大鼠神经元损伤和空间记忆障碍等行为学缺陷[29]。因此，氧化应激可能是微塑料神经毒性的重要机制之一。

2.神经炎症：神经胶质细胞的过度激活是神经炎症的特征性标志之一[30]。微塑料能够穿透小鼠血脑屏障并在脑组织中蓄积，诱导小胶质细胞活

化，进而导致神经元损伤[31]。另一项研究发现，将大鼠长期暴露于PS-NPs后，其杏仁核和血清中的TNF-α、IL-1β、IL-6等炎性因子水平显著升高，进而诱导杏仁核结构损伤和焦虑相关行为[32]。体外实验进一步验证了这一机制。Sun等[33]将小鼠神经小胶质细胞暴露于纳米塑料中，发现纳米塑料可侵入细胞，激活炎性小体，诱导大量炎性因子的释放。此外，微塑料暴露可能通过脑–肠轴调控途径诱导中枢神经系统神经炎性反应的发生。微塑料可通过诱导溶酶体损伤导致肠道巨噬细胞活化，产生大量的IL-1，这种来自肠道的IL-1信号传导会导致大脑小胶质细胞激活和辅助性T细胞17(T helper cell 17, Th17)分化，进而导致小鼠的认知功能障碍和短期记忆下降[34]。因此，微塑料暴露可通过直接(血脑屏障渗透)和间接(脑–肠轴)途径激活神经炎性反应，进而引发多层次的神经毒性效应。

3.神经递质失调：神经递质作为化学信使，在整个神经系统的信息处理中起着至关重要的作用，神经递质系统的失调通常与特定的神经系统疾病有关[35]。现有研究证实，微塑料可通过干扰神经递质稳态引发神经毒性效应，其作用机制已在多物种模型中得到系统验证。在无脊椎动物模型中，Chen等[36]对秀丽隐杆线虫的研究显示，暴露于光老化聚苯乙烯显著改变了其体内5–羟色胺能、谷氨酸能、多巴胺能和氨基丁酸的神经递质水平，其头部抖动、身体弯曲等异常运动行为增多。脊椎动物研究中，Huang等[37]在七彩神仙鱼中观察到纳米塑料暴露可显著升高脑内大脑中乙酰胆碱、多巴胺和GABA的浓度，这些改变与其游泳速度降低和捕食成功率下降显著相关。哺乳动物层面的证据来自Tian等[38]的大鼠神经发育毒性研究，妊娠期PS-NPs暴露可导致子代出现大脑皮层单胺类神经递质和海马氨基酸类神经递质水平异常，进而引发抗焦虑样行为和空间记忆缺陷。总而言之，微塑料能够引发动物脑内神经递质失衡，进而对动物神经系统造成危害，并对其学习记忆能力、情绪表现以及行为模式产生一系列不良影响。

三、总结与展望

目前，关于微塑料对动物神经发育行为学的毒性作用及相关机制研究已经取得了一定进展。但需要指出的是，现阶段对于微塑料的毒性作用和机制研究基本还处于实验室层面，且多采用PS-MPs和纳米塑料进行研究，在微塑料不同暴露途径的风险评估、塑料颗粒老化及基团修饰后的危害性、与其他污染物共同暴露和如何准确检测生物体内的微塑料等多领域仍有待探索。另外，在今后的研究中还需不断改进实验方法，以更好地模拟环境中生物的微塑料暴露情况。当前微塑料毒性的研究主要基于动物实验，微塑料对于人类神经系统的危害性研究和机制尚处于起步阶段，未来还需将相关研究结果与流行病学研究相结合，以更全面地评估微塑料暴露对人类神经系统的危害，为防治微塑料相关神经疾病提供新的思路。

利益冲突 文章所有作者共同认可文章无相关利益冲突

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