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·综 述·

炎症因子与近视关联的研究进展

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【摘要】 目前儿童青少年近视病因与发病机制尚未明确, 炎症因子作为生物体内重要的调节介质, 其在近视发生发展中的潜在作用引起越来越多的关注。研究对全身性炎症和眼内炎症状态与近视的关联进行阐述, 探讨近视发病的炎症机制及靶向调控相关信号通路在近视治疗中的干预策略, 为儿童青少年近视防控提供新思路。

【关键词】 炎症趋化因子类; 近视; 研究; 健康促进

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Research progress on the association between inflammatory factors and myopia

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【**Abstract**】 The etiology and pathogenesis of myopia among children and adolescents remain unclear. As crucial regulatory mediators in the body, inflammatory cytokines have drawn increasing attention for their potential role in the onset and progression of myopia. The study examines the relationship between systemic inflammation and intraocular inflammation and myopia, explores the inflammatory mechanisms underlying myopia development, and discusses intervention strategies targeting related signaling pathways for myopia treatment. It aims to provide new insights for the prevention and control of myopia in children and adolescents.

【**Keywords**】 Chemokines; Myopia; Research; Health promotion

近年来, 近视已成为全球范围内日益严重的公共卫生问题[1-2]。近视主要由遗传和环境因素共同作用引发[3]。然而, 最新研究提示, 近视的发生不仅是视觉行为和屈光调节的功能性紊乱, 更涉及到眼组织的复杂生物分子机制, 在这一过程中, 炎症反应作为重要免疫调节机制, 可能通过参与巩膜重塑、细胞外基质降解、局部免疫微环境失衡等方式促进眼轴延长和近视进展[4]。多项研究发现, 近视眼组织中多种炎症因子表达上调, 可能介导相关信号通路激活, 导致组织结构与功能改变[5-7]。本文对炎症因子与近视的关联及其在近视发生发展中的潜在机制进行综述, 旨在为儿童青少年近视防控提供参考依据。

1 炎症因子与近视的关联

1.1 全身性炎症与近视的关联 全身性炎症与近视发生发展存在关联。一项双向双样本孟德尔随机化研究发现, 趋化因子 CXCL9、CXCL11 是近视的危险因素, 而白细胞介素 5 是近视的保护因素, 该研究进一步通过 2 个独立队列的验证分析证实, 高度近视患者存在促炎症状态, 主要表现为血浆 CXCL9、CXCL11 水平显著升高[8]。另一项双样本孟德尔随机化研究也发现, 血管内皮生长因子 A(vascular endothelial growth factor A, VEGF-A)、单核细胞趋化蛋白 2 等炎症标志物是近视和屈光不正的风险因素[9]。对照实验结果表明, 全身炎症标志物高敏 C 反应蛋白、补体 C3 和总补体活性 CH50 在高度近视发展中有重要作用[10]。较高的白细胞计数也与近视和高度近视患病率增加相关[11], 高度近视的发展可能与中性粒细胞与淋巴细胞比值以及血小板与淋巴细胞比值有关[12-13]。基于美国国家健康与营养调查数据分析结果显示, 饮食炎症指数与青少年近视患病率呈正相关, 提示促炎饮食可能通过引发全身性炎症来增加近视风险[14]。

1.2 眼内炎症状态与近视的关联 眼内微环境中也发现了与近视相关的炎症反应。横断面研究发现, 近

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视患者房水中白细胞介素 6(interleukin-6, IL-6)、基质金属蛋白酶 2(matrix metalloproteinase 2, MMP-2)与眼轴长度均呈正相关,而总抗氧化能力水平与眼轴长度呈负相关,提示轻度眼内炎症和氧化应激失衡可能与近视的发生有关[15]。另一项研究发现高度近视患者房水中 IL-6、白细胞介素 8(interleukin-8, IL-8)和血管生成素 2 水平更高、VEGF-A 水平更低,表明眼内的炎症状态与高度近视存在关联[16]。回顾性研究也发现,高度近视患者玻璃体中干扰素-γ(interferon-γ, IFN-γ)、IL-6、IFN-γ 诱导蛋白 10、巨噬细胞炎症蛋白 1α 和嗜酸性粒细胞趋化因子 5 种炎症因子均高于对照组,提示高度近视患者眼中存在炎症状态的升高[17]。横断面研究通过对印度儿童的无创泪液分析发现,高度近视儿童的泪液中肿瘤坏死因子 α(tumor necrosis factor-α, TNF-α)和细胞间黏附分子 1 等炎症因子升高,且与干眼症状相关,表明眼表局部炎症可能是儿童近视发展的潜在风险因素[18]。双向孟德尔随机化分析联合动物实验研究证实炎症因子是近视发展的潜在病因,其中白细胞介素 2 水平升高与近视风险增加之间存在潜在因果关系[19]。未来需要更多纵向研究进一步明确炎症因子与近视之间的因果关联。

2 炎症因子与近视关联的可能机制

2.1 *炎症因子与巩膜重塑* 巩膜在近视发展过程中会发生一系列生物学改变,如胶原蛋白积累减少、胶原蛋白框架合成减速、加速降解以及细胞外基质成分改变等,这些改变称为巩膜重塑[20]。巩膜重塑能够改变眼球的生物力学特性,在近视的发生发展中起关键作用[21]。在巩膜重塑发展过程中,MMP-2 的上调是关键分子事件,可促进动物巩膜框架重组和细胞外基质重塑,其水平增加与眼轴长度延长密切相关[22]。

越来越多的研究发现,IL-6 在巩膜重塑的发生过程中起重要作用。日本一项研究发现,在小鼠模型的近视诱导过程中,巩膜和脉络膜中的 IL-6 表达显著增加,且这一变化与 MMP-2 的激活密切相关;IL-6 通过激活 MMP-2,间接促使巩膜的薄化和眼轴延长,从而加速近视的进展[23]。另一项研究发现,模拟近视在缺氧条件下巩膜成纤维细胞中的 IL-6 表达显著上升,IL-6 可能通过影响巩膜成纤维细胞的增殖、分化和凋亡,促进 I 型胶原蛋白的降解,进而加速巩膜变薄,这一变化直接与眼轴的延长相关,加剧近视发生的进展,IL-6 还通过调控转化生长因子-β1(transforming growth factor-β1, TGF-β1)/Smad 家族成员 2(Smad family member 2, Smad2)/MMP-2 通路的活性,进一步加剧巩膜变薄[24]。

2.2 *细胞信号通路的激活* 树鼩模型研究发现,形觉剥夺性近视(form-deprivation myopia, FDM)7 d 组和 14 d组眼屈光度分别从(+6.6±0.3)(+6.4±0.3)D 降至(+4.0±0.5)(+5.0±0.3)D,FDM 眼较对照组 TNF-α、IL-6、IL-8、单核细胞趋化蛋白 1(monocyte chemoattractant protein-1, MCP-1)和核因子 κB(nuclear factor kappa-B, NF-κB)水平升高,FDM 眼 MMP-2 表达的增加大于对侧和对照眼,而 I 型胶原蛋白表达下调;免疫组化分析结果进一步显示,MCP-1、转化生长因子-β(transforming growth factor-β, TGF-β)和 IL-8 通过激活 NF-κB 通路引发炎症反应,增加促炎细胞因子 TNF-α 和 IL-6 的表达,并同时激活 MMP-2 和下调 I 型胶原蛋白表达促进近视进展,提示慢性炎症可能在树鼩 FDM 中起关键致病作用[25]。另一项树鼩单眼模型研究发现,玻璃体注射 TGF-β 组可促进近视进展,进一步提示玻璃体注射 TGF-β 可上调 MMP-2 和 NF-κB 水平、下调 I 型胶原蛋白水平,表明 MMP-2 可能通过 TGF-β 诱导的 NF-κB 信号通路激活介导 I 型胶原蛋白的降解,促进近视进展[26]。叙利亚仓鼠 FDM 模型也发现炎症相关转录因子原癌基因 *c-FOS* 和 NF-κB 以及炎性细胞因子 IL-6、TNF-α、白细胞介素 1β(interleukin-1β, IL-1β)、TGF-β 和 MMP-2 表达上调,而抗炎细胞因子 IL-10 水平降低,揭示 NF-κB 信号通路被炎症因子激活后,通过上调 MMP-2 等靶基因表达促进巩膜重塑与眼轴延长,可能是驱动近视发生发展的关键炎症机制[5]。

NOD 样受体蛋白 3(NOD-like receptor protein 3, NLRP3)炎症小体及其信号通路可能也参与了近视进展。Chen 等[27]研究发现,小鼠 FDM 模型巩膜中 NLRP3 表达显著上调,NLRP3 能促进 IL-1β 的激活,从而诱导 MMP-2 的表达增加,并下调 I 型胶原蛋白,导致巩膜细胞外基质重塑、结构减弱、眼轴延长,最终推动近视发展。Xiao 等[28]研究反向验证了可以通过切断 NLRP3 通路上游补体系统的激活信号,减弱 NLRP3 通路的激活,从而导致 MMP-2 上调受限、胶原降解减少,近视进展减缓。因此,抑制 NF-κB 和 NLRP3 通路活性有望成为近视治疗的新靶点。

3 炎症抑制与近视

降低炎症水平可能是抑制近视发展的重要途径,研究表明,在 TNF-α 给药诱导的动物近视模型中,衰变加速因子的应用能够抑制补体系统激活,降低 MMP-2和 TGF-β 等特异性细胞因子的表达,从而下调炎症水平并抑制近视的发展[29]。日本虎杖提取物和夏枯草提取物在仓鼠单眼形觉剥夺模型中可以通过降低视网膜色素上皮细胞中 IL-6、IL-8 和 TNF-α

的表达，并通过减弱蛋白激酶 B（protein kinase B，PKB，又称 AKT）和活化 NF-κB 通路的磷酸化来抑制炎症，从而减缓近视进展[30]。

此外，在白藜芦醇处理的仓鼠单眼形觉剥夺模型中发现，近视相关的组织重塑蛋白和炎性细胞因子（NF-κB、TGF-β、MMP2、TNF-α、IL-6 和 IL-1β）的表达显著降低，I 型胶原蛋白的表达增加，这些发现表明白藜芦醇会通过阻断相关信号通路来抑制炎症作用，从而改善近视的发展[31]。不仅如此，一项对仓鼠单眼形觉剥夺的研究也表明，地醋瑞因能够抑制近视相关 TGF-β1 和 MMP-2 的水平，增加 I 型胶原蛋白的表达，同时降低视网膜上皮细胞中 IL-6、IL-8 和 MCP-1 的表达，并通过减弱 AKT 和 NF-κB 通路的磷酸化，抑制炎症反应，从而减轻视网膜炎症以减缓近视进展[32]。提示靶向炎症信号通路可能为近视干预提供新策略。

4　小结

近视发生发展是一个复杂的过程，炎症因子可能在近视的发病机制中扮演着重要角色，尽管已有多项研究揭示炎症因子在近视中的潜在作用，但目前证据仍以观察性研究为主，尚未能够确立炎症因子与近视发生发展的因果关系。未来应进一步开展纵向和机制学研究，明确特定炎症通路在近视发生中的因果作用及具体机制，进一步推动靶向炎症通路的干预研究，评估抗炎药物和天然产物在近视防控中的应用潜力与安全性。同时，应积极探索炎症因子作为近视早期生物标志物的可能性，为近视防控提供新的理论基础和实践指导。炎症因子的深入研究不仅有助于理解近视的发病机制，也为防控策略从传统光学矫正向病因干预转变提供了理论依据，为中国儿童青少年近视防控提供新的思路和方法。

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