·论著·

高压氧调控AMPK/SIRT1/PGC1α信号通路对急性一氧化碳中毒迟发性脑病大鼠神经元损伤的影响

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摘要 目的 探讨高压氧(HBO)调控单磷酸腺苷活化蛋白激酶(AMPK)/沉默信息调节因子2同系物1(SIRT1)/氧化物酶体增殖物激活受体γ共激活剂1α(PGC-1α)信号通路对急性一氧化碳中毒迟发性脑病(DEACMP)大鼠神经元损伤的影响。**方法** 构建DEACMP大鼠模型,并将其分为DEACMP组,HBO组(建模1 h后,按2.0 ATA、稳压时间60 min进行HBO治疗),HBO+Compound C组(HBO治疗+腹腔注射2 mg/kg AMPK抑制剂Compound C)。对各组大鼠进行mNSS评分,用Morris水迷宫实验检测神经功能缺损,ELISA检测血清白细胞介素(IL)-1β、肿瘤坏死因子α(TNF-α)、IL-6水平,HE染色检测海马组织CA1区病理组织变化,TUNEL染色观察海马组织神经元凋亡,Western blotting检测海马组织蛋白表达。**结果** DEACMP组大鼠海马组织CA1区可见神经元核皱缩、细胞数量减少、排列紊乱等损伤;HBO组海马组织CA1区损伤明显减轻;HBO+Compound C组海马组织CA1区损伤进一步加重。DEACMP组mNSS评分、逃避潜伏期、IL-1β、TNF-α、IL-6水平及凋亡率高于NC组,跨越平台次数、AMPK、SIRT1、PGC1α表达低于NC组($P < 0.05$);HBO组mNSS评分、逃避潜伏期、IL-1β、TNF-α、IL-6水平及凋亡率低于DEACMP组,跨越平台次数、AMPK、SIRT1、PGC1α高于DEACMP组($P < 0.05$);HBO+Compound C组mNSS评分、逃避潜伏期、IL-1β、TNF-α、IL-6水平及凋亡率高于HBO组,跨越平台次数、AMPK、SIRT1、PGC1α低于HBO组($P < 0.05$)。**结论** HBO可能通过激活AMPK/SIRT1/PGC1α信号通路改善DEACMP大鼠的神经元损伤。

关键词 高压氧;单磷酸腺苷活化蛋白激酶;沉默信息调节因子2同系物1;氧化物酶体增殖物激活受体γ共激活剂1α;急性一氧化碳中毒迟发性脑病;神经元损伤
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Effect of hyperbaric oxygen on neuronal damage in rats with delayed encephalopathy after acute carbon monoxide poisoning via regulating the AMPK/SIRT1/PGC1α signaling pathway

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Abstract Objective To explore the effect of hyperbaric oxygen (HBO) treatment on neuronal damage in rats with delayed encephalopathy after acute carbon monoxide poisoning (DEACMP), mediated by the regulation of the adenosine monophosphate activated protein kinase (AMPK)/silent mating type information regulation 2 homolog 1 (SIRT1)/peroxisome proliferator activated receptor γ coactivator-1α (PGC-1α) signaling pathway. **Methods** DEACMP model rats were induced and separated into the DEACMP, HBO (HBO therapy performed with 2.0 ATA and stable pressure for 60 min 1 h after modeling), and HBO+Compound C (HBO therapy was performed with intraperitoneal injection of 2 mg/kg AMPK inhibitor Compound C) groups. Rats in each group were scored using the mNSS. The Morris water maze test was applied to measure neurological deficits. ELISA was conducted to measure serum IL-1β, TNF-α, and IL-6 levels. HE staining was conducted to detect pathological changes in the hippocampal tissue. TUNEL staining was applied to observe neuronal apoptosis in the hippocampal tissue. Western blotting was used to measure the AMPK, SIRT1, and PGC1α proteins in hippocampal tissue. **Results** The DEACMP group showed damage in the hippocampal tissue, including neuronal nucleus shrinkage, reduced cell count, and disordered arrangement. The HBO group showed a significant reduction in this hippocampal tissue damage, while damage to the hippocampal tissue in the HBO+Compound C group was further worsened. The DEACMP group had higher mNSS scores, escape latency,

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IL-1β, TNF-α, IL-6 levels, and apoptosis rate, as well as a lower number of platform crossings, AMPK, SIRT1, and PGC1α than the NC group ($P < 0.05$). The HBO group had a lower mNSS score, escape latency, IL-1β, TNF-α, IL-6 levels, and apoptosis rate, as well as a higher number of platform crossings; and AMPK, SIRT1, and PGC1α levels than the DEACMP group ($P < 0.05$). The HBO+Compound C group had a higher mNSS score, escape latency, IL-1β, TNF-α, and IL-6 levels, and apoptosis rate, as well as lower number of platform crossings; and AMPK, SIRT1, and PGC1α levels than the HBO group ($P < 0.05$). **Conclusion** HBO may improve neuronal damage in DEACMP rats by activating the AMPK/SIRT1/PGC1α signaling pathway.

Keywords hyperbaric oxygen; adenosine monophosphate activated protein kinase; silent mating type information regulation 2 homolog 1; peroxisome proliferator activated receptor γ coactivator-1α; delayed encephalopathy after acute carbon monoxide poisoning; neuronal damage

急性一氧化碳中毒(acute carbon monoxide poisoning, ACOP)是由过量一氧化碳(carbon monoxide, CO)吸入引起的缺氧疾病,是中毒相关死亡的最常见原因之一,全球ACOP累计发病率为137/1 000 000,死亡率为4.6/1 000 000[1]。急性一氧化碳中毒迟发性脑病(delayed encephalopathy after acute carbon monoxide poisoning, DEACMP)是ACOP最常见和最严重的并发症之一,发病率为13%~50%,死亡率可达31%[2]。DEACMP与神经元损伤密切相关[3]。高压氧(hyperbaric oxygen, HBO)是DEACMP综合治疗策略的核心,能有效缓解DEACMP患者的症状,减少脑白质病变[4]。单磷酸腺苷活化蛋白激酶(adenosine monophosphate activated protein kinase, AMPK)是调节生物能量代谢的关键分子,可通过激活沉默信息调节因子2同系物1(silent mating type information regulation 2 homolog 1, SIRT1),上调氧化物酶体增殖物激活受体γ共激活剂1α(peroxisome proliferator activated receptor γ coactivator-1α, PGC-1α)的表达,在调节线粒体生物发生中至关重要[5]。研究[6]表明,AMPK/SIRT1/PGC-1α信号通路的激活可促进线粒体生物发生,从而改善阿尔茨海默病患者的认知障碍和神经元损伤。因此,本研究拟探讨HBO调控AMPK/SIRT1/PGC1α信号通路对DEACMP神经元损伤的影响。

1　材料与方法

1.1　材料

1.1.1　实验动物:雄性成年SPF级Wistar大鼠(6~8周龄,体重180~230 g)48只,购自维通达(固安)生物技术有限公司,生产许可编号SCXK(冀)2024-002。在标准条件下饲养,室温18~23 ℃,12 h明暗循环,自由饮水和摄食。本研究获得维通达(固安)生物技术有限公司动物伦理委员会批准(WTD-2024071267)。

1.1.2　主要试剂与仪器:AMPK抑制剂Compound C(货号154127-19-2,北京孚博生物科技有限公司);肿瘤坏死因子α(tumour necrosis factor-α, TNF-α)、白细胞介素-1β(interleukin-1 β, IL-1β) ELISA试剂盒(货号SND-R635、SND-R418,滁州仕诺达生物科技有限公司);HE染色试剂盒(货号F4713,上海远慕生物科技有限公司);TUNEL染色试剂盒(货号F4708-50D,上海岑特生物科技有限公司);β肌动蛋白(β-actin)、AMPK、SIRT1、PGC1α、辣根过氧化物酶(货号ab184705、ab271188、ab32441、ab313559、ab6721,英国abcam公司);酶标仪(K3 Pro,广东丹利科技有限公司)。

1.2　实验方法

1.2.1　动物模型制备、分组和HBO治疗:采用改良式间隔腹腔注射法构建DEACMP大鼠模型,36只大鼠腹腔注射CO气体(120 mL/kg,纯度99.99%)后,按该剂量的2/3追加注射3次。另选择12只大鼠作为对照组(NC组),用同样方式注射等量空气。染毒后1 h开始连续监测3次(间隔4 h监测1次)大鼠尾静脉血碳氧血红蛋白(carbonyl hemoglobin, COHb)浓度>50%,染毒后5 d进行Morris水迷宫实验,大鼠出现认知障碍,判定模型构建成功[7]。将建模成功的大鼠分为DEACMP组,HBO组[建模1 h后,按2.0 绝对大气压(atmosphere absolute, ATA),稳压时间60 min进行HBO治疗[8]],HBO+Compound C组(HBO治疗+腹腔注射2 mg/kg Compound C [9]),每组12只,每天治疗和注射1次,共20 d。

1.2.2　改良神经损伤严重程度评分(modified neurological severity score, mNSS)评估神经功能:治疗结束后,采用mNSS从3个方面(运动、感觉、肢体反射)对各组大鼠神经功能进行评估,最高为18分。

1.2.3　Morris水迷宫实验检测神经功能缺损:治疗结束后进行Morris水迷宫实验。将大鼠随机从4个地

点置于水迷宫中，学习如何找到逃生平台（4次/d）。若未在2 min内找到逃生平台，则将其放置在逃生平台上10 s。5 d后，选择2 min内能找到逃生平台的大鼠进行后续实验。

1.2.4　ELISA检测血清IL-1β、TNF-α、IL-6水平：麻醉大鼠收集腹主动脉血，分别按相应ELISA试剂盒说明书进行检测。

1.2.5　HE染色检测海马组织CA1区病理变化：麻醉处死大鼠，取海马组织CA1区，于4%多聚甲醛中固定过夜，制成5 μm厚切片，经HE染色后在光学显微镜下观察。

1.2.6　TUNEL染色观察大鼠海马组织神经元凋亡：取大鼠海马组织切片，加入蛋白酶K，37 ℃孵育30 min，用PBS洗涤后，将TdT酶反应液和链霉亲和素–HRP表位液分别在37 ℃无光的条件下作用于切片30 min，用PBS洗涤，DAB染色，经脱水、清理、中性树脂封片后，在光学显微镜下观察。

1.2.7　Western blotting检测海马组织中蛋白表达：用RIPA裂解液处理海马组织，离心取上清，采用BCA法测定蛋白浓度。蛋白上样行15% SDS-PAGE。转膜，用10%脱脂牛奶室温封闭2 h。加β-actin（1 ∶ 1 000）、AMPK（1 ∶ 1 000）、SIRT1（1 ∶ 20 000）、PGC1α（1 ∶ 1 000）一抗4 ℃孵育过夜。用二抗（1 ∶ 2 000）孵育1 h。ECL可视化，用ImageJ软件进行分析。

1.3　统计学分析

采用SPSS 26.0软件进行统计学分析。符合正态分布的计量资料以$\bar{x} \pm s$表示，多组间及组间两两比较采用单因素方差分析和SNK-q检验。$P < 0.05$为差异有统计学意义。

2　结果

2.1　HBO对DEACMP大鼠mNSS的影响

DEACMP组mNSS（14.17 ± 1.76）高于NC组（0.00 ± 0.00），HBO组mNSS（5.38 ± 1.05）低于DEACMP组，HBO+Compound C组mNSS（11.29 ± 1.47）高于HBO组，差异均有统计学意义（均$P < 0.05$）。

2.2　HBO对DEACMP大鼠认知能力的影响

DEACMP组逃避潜伏期高于NC组，跨越平台次数低于NC组（$P < 0.05$）；HBO组逃避潜伏期低于DEACMP组，跨越平台次数高于DEACMP组（$P < 0.05$）；HBO+Compound C组逆转HBO组上述变化（$P < 0.05$）。见表1。

表1　各组大鼠逃避潜伏期、跨越平台次数比较

Tab.1　Comparison of the escape latency and the number of platform crossings in rats of each group

Group	n	Escape latency (s)	Number of platform crossings
NC	12	9.15 ± 2.26	14.49 ± 1.72
DEACMP	12	62.39 ± 6.35[1)]	3.15 ± 0.83[1)]
HBO	12	15.27 ± 3.11[2)]	12.06 ± 1.37[2)]
HBO+Compound C	12	49.18 ± 5.26[3)]	5.47 ± 0.96[3)]

1) $P < 0.05$ vs. NC group；2) $P < 0.05$ vs. DEACMP group；3) $P < 0.05$ vs. HBO group.

2.3　HBO对DEACMP大鼠血清IL-1β、TNF-α、IL-6水平的影响

DEACMP组血清IL-1β、TNF-α、IL-6水平高于NC组，HBO组血清IL-1β、TNF-α、IL-6水平低于DEACMP组，HBO+Compound C组逆转HBO组的上述作用，差异均有统计学意义（均$P < 0.05$）。见表2。

表2　各组大鼠血清IL-1β、TNF-α、IL-6水平比较（pg/mL）

Tab.2　Comparison of the levels of IL-1β，TNF-α and IL-6 in the serum of rats in each group (pg/mL)

Group	n	IL-1β	TNF-α	IL-6
NC	12	45.19 ± 8.31	18.73 ± 3.05	4.11 ± 1.73
DEACMP	12	128.74 ± 13.19[1)]	56.92 ± 5.97[1)]	27.85 ± 2.97[1)]
HBO	12	61.48 ± 10.02[2)]	22.05 ± 4.32[2)]	6.29 ± 1.92[2)]
HBO+Compound C	12	103.52 ± 12.48[3)]	48.31 ± 5.12[3)]	19.02 ± 2.34[3)]

1) $P < 0.05$ vs. NC group；2) $P < 0.05$ vs. DEACMP group；3) $P < 0.05$ vs. HBO group.

2.4　HBO对DEACMP大鼠海马组织CA1区病理变化的影响

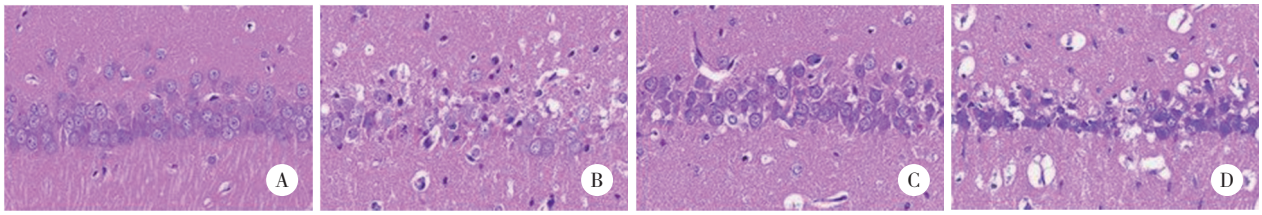
NC组海马组织CA1区结构清晰，神经元排列整齐；DEACMP组海马组织CA1区出现神经元核皱缩、细胞数量减少、排列紊乱等损伤；HBO组海马组织CA1区损伤明显减轻；HBO+Compound C组海马组织损伤进一步加重。见图1。

2.5　HBO对DEACMP大鼠海马组织神经元凋亡的影响

DEACMP组凋亡率（23.10% ± 2.48%）高于NC组（1.29% ± 0.31%），HBO组凋亡率（8.19% ± 1.23%）低于DEACMP组，HBO+Compound C组凋亡率（16.21% ± 1.79%）高于HBO组（均$P < 0.05$）。见图2。

2.6　HBO对DEACMP大鼠海马组织中AMPK、SIRT1、PGC1α蛋白表达的影响

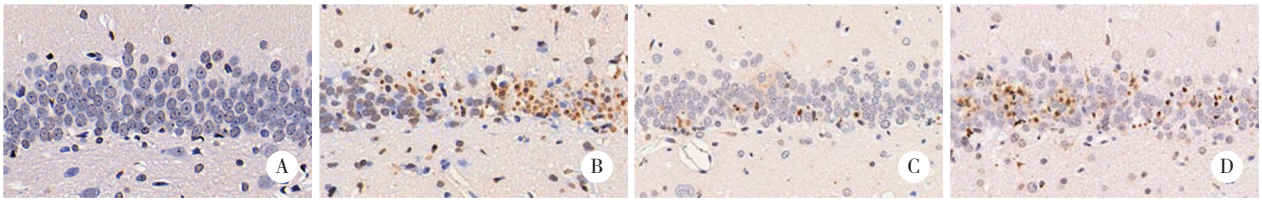
DEACMP组AMPK、SIRT1、PGC1α蛋白表达低于NC组，HBO组AMPK、SIRT1、PGC1α蛋白表达高于DEACMP组，HBO+Compound C组AMPK、SIRT1、PGC1α蛋白表达低于HBO组，差异均有统计学意义（均$P < 0.05$）。见图3。



A，NC group；B，DEACMP group；C，HBO group；D，HBO+Compound C group.

图1　各组大鼠海马组织CA1区病理变化　HE × 400

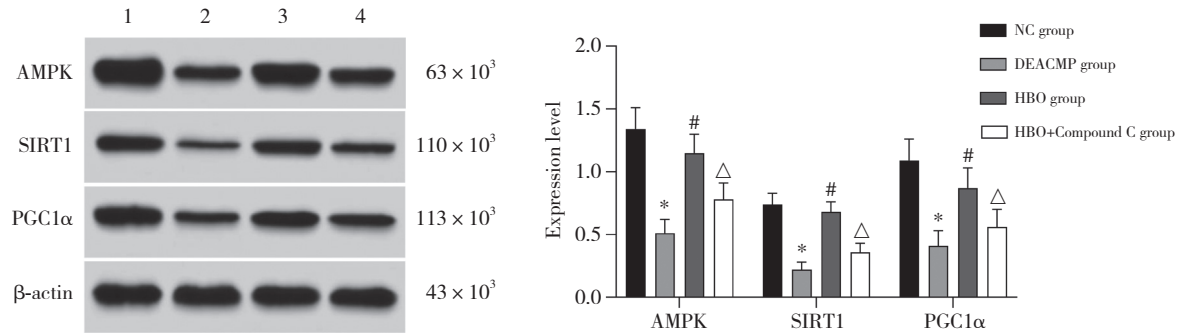
Fig.1　Pathological changes in the CA1 area of hippocampus of rats in each group　HE × 400



A，NC group；B，DEACMP group；C，HBO group；D，HBO+Compound C group.

图2　各组大鼠海马组织神经元凋亡情况　TUNEL × 400

Fig.2　The apoptosis status of neurons in the hippocampal tissues of rats in each group　TUNEL × 400



1，NC group；2，DEACMP group；3，HBO group；4，HBO+Compound C group. *$P < 0.05$ vs. NC group；#$P < 0.05$ vs. DEACMP group；△$P < 0.05$ vs. HBO group. $n = 12$.

图3　HBO对各组大鼠海马组织中AMPK、SIRT1、PGC1α蛋白表达的影响

Fig.3　The influence of HBO on the protein expression of AMPK，SIRT1 and PGC1α in the hippocampal tissue of rats in each group

3　讨论

DEACMP是ACOP最常见的并发症之一[10]，其特征是在ACOP 2~60 d后出现认知功能障碍、人格改变、精神障碍等神经和精神症状[11]。CO与血红蛋白的亲和力比氧与血红蛋白的亲和力强200~300倍，从而阻碍了氧的输送和利用，导致全身组织缺氧[12]。中枢神经系统神经元尤其易受缺血和缺氧的影响，缺氧可诱导神经元损伤和死亡，损害神经元功能[13-14]。本研究通过构建DEACMP大鼠模型发现，DEACMP大鼠海马组织出现神经元损伤，mNSS增加，逃避潜伏期延长，血清IL-1β、TNF-α、IL-6水平及细胞凋亡率升高，跨越平台次数减少，提示DEACMP后缺氧导致细胞炎症反应，进一步引起神经元凋亡，导致神经受损。

CO中毒的治疗包括从COHb中排出CO，补充氧，以及一般支持治疗。HBO治疗可以加速COHb的消除，常压下给予100%氧气后，COHb的消除半衰期（在室内空气中约为320 min）缩短约5倍，能有效缓解DEACMP患者的症状[15]。HBO在减轻缺血缺氧损伤、减少炎症反应和细胞凋亡方面具有明确的作用[4,16]。HBO治疗可有效改善DEACMP患者的认知功能、日常行为能力、精神行为症状及整体状态变化，改善患者预后[17]。本研究结果发现，HBO可降低DEACMP大鼠炎症反应，改善神经元损伤，但其具体分子机制尚不清晰。

AMPK/SIRT1/PGC1α信号通路可介导线粒体功能，通过调节多种生物学行为，减轻神经元损伤[6,18]。研究[19]发现，激活AMPK/SIRT1/PGC1α信号通路可通过拮抗氧化应激和维持线粒体功能，减少神经元凋亡，改善七氟烷麻醉老龄大鼠的认知功能，减轻神经元损伤。ELESAWY等[20]发现，依泽替米贝通过激活AMPK/SIRT-1/PGC1α信号通路，增强细胞自噬，减弱细胞凋亡，对鱼藤酮诱导的帕金森病具有神经保护作用。另有研究[21]发现，小鼠产前暴露于丙戊酸盐会导致焦虑和自闭症样行为，这可能是由于AMPK/SIRT1/PGC1α信号通路被抑制所致。胡滨等[22]发现，川穹嗪通过上调偏头痛大鼠模型的SIRT1/AMPK/PGC1α信号通路，抑制炎症反应，减少神经元凋亡，改善神经元损伤。本研究发现，DEACMP大鼠海马组织中AMPK/SIRT1/PGC1α信号通路蛋白低表达，而HBO处理可激活AMPK/SIRT1/PGC1α信号通路，改善大鼠神经元损伤，而AMPK抑制剂可抵消上述保护效应，提示激活 AMPK/SIRT1/PGC1α信号通路是HBO发挥神经保护作用的重要机制。

综上所述，本研究发现，HBO可能通过激活AMPK/SIRT1/PGC1α信号通路，改善DEACMP大鼠海马神经元损伤，其具体机制有待进一步研究。

参考文献：

[1] WANG YJ, ZHOU ZZ, ZHANG DL, et al. Predictors of delayed encephalopathy after acute carbon monoxide poisoning: a literature review [J]. Front Med, 2025, 12: 1559264. DOI: 10.3389/fmed.2025.1559264.

[2] XIANG WP, YANG ZG, XUE H, et al. P2Y12 receptor-mediated microglia activation involved in delayed encephalopathy after acute carbon monoxide poisoning [J]. Aging, 2021, 13 (4): 6134-6143. DOI: 10.18632/aging.202607.

[3] MU YH, GAO N, WANG YT, et al. High-density lipoprotein cholesterol protects against delayed encephalopathy after acute carbon monoxide poisoning [J]. Toxicol Appl Pharmacol, 2026, 506: 117663. DOI: 10.1016/j.taap.2025.117663..

[4] HUANG FL, YANG L, TAN Z, et al. Prognostic factors of hyperbaric oxygen therapy for patients with delayed encephalopathy after acute carbon monoxide poisoning [J]. Heliyon, 2022, 8 (12): e12351. DOI: 10.1016/j.heliyon.2022.e12351.

[5] WANG HQ, DOU SS, ZHU JG, et al. Ghrelin protects against rotenone-induced cytotoxicity: involvement of mitophagy and the AMPK/SIRT1/PGC1α pathway [J]. Neuropeptides, 2021, 87: 102134. DOI: 10.1016/j.npep.2021.102134.

[6] ZHU C, ZHANG Z, ZHU YS, et al. Study on the role of Dihuang Yinzi in regulating the AMPK/SIRT1/PGC-1α pathway to promote mitochondrial biogenesis and improve Alzheimer's disease [J]. J Ethnopharmacol, 2025, 337 (Pt 2): 118859. DOI: 10.1016/j.jep.2024.118859.

[7] 张谦，赵俊喜，景苗苗，等. 补阳还五汤对一氧化碳中毒迟发性脑病大鼠氧化损伤及Nrf2/HO-1信号通路的影响 [J]. 西部中医药，2023，36 (3)：35-40. DOI：10.12174/j.issn.2096-9600.2023.03.07.

[8] 周磊，范茂丹，斯银平，等. 高压氧治疗对一氧化碳中毒后迟发性脑病大鼠海马组织中炎症因子表达的影响 [J]. 心脑血管病防治，2021，21 (1)：35-38，43. DOI：10.3969/j.issn.1009-816x.2021.01.006.

[9] 李庆贵，陈康，郭召，等. 汉黄芩素调节AMPK/SIRT1信号通路对骨质疏松大鼠骨折愈合的影响 [J]. 实用医学杂志，2023，39 (4)：410-416. DOI：10.3969/j.issn.1006-5725.2023.04.004.

[10] LIU XJ, ZENG J, ZHANG XL, et al. The relationship between cadherin polymorphisms and the risk of delayed encephalopathy after acute carbon monoxide poisoning in the Chinese Han population [J]. Behav Neurol, 2022, 2022: 3155703. DOI: 10.1155/2022/3155703.

[11] XU LL, LIU XJ, ZHAO J, et al. Association between neuron-specific enolase gene polymorphism and delayed encephalopathy after acute carbon monoxide poisoning [J]. Behav Neurol, 2020, 2020: 8819210. DOI: 10.1155/2020/8819210.

[12] LIU JZ, SI ZH, LIU J, et al. Clinical and imaging prognosis in pa-

（下转第569页）

225-229. DOI:10.16386/j.cjpccd.issn.1004-6194.2024.03.013.
[11] 王海滨,李平,张志刚,等. 连翘苷调节MAPK/NF-κB/NLRP3信号通路对膝骨性关节炎大鼠软骨损伤的影响[J]. 国际检验医学杂志,2023,44(15):1902-1907. DOI:10.3969/j.issn.1673-4130.2023.15.021.
[12] 唐晓栋,赵庆,兰晓飞,等. 豨莶草调控sirt1/FOXO1通路对膝骨关节炎大鼠软骨损伤的影响[J]. 中国免疫学杂志,2020,36(4):439-444. DOI:10.3969/j.issn.1000-484X.2020.04.011.
[13] WANG WY,CHU YR,LU YK,et al. Skatole alleviates osteoarthritis by reprogramming macrophage polarization and protecting chondrocytes[J]. Research,2025,8:0604. DOI:10.34133/research.0604.
[14] 李欣,曾阳俊,汪磊,等. 蜂毒肽在类风湿性关节炎领域的研究进展[J]. 中国医院药学杂志,2024,44(17):2062-2065. DOI:10.13286/j.1001-5213.2024.17.17.
[15] 汤发强,吴宏,郑建章,等. 蜂毒肽对大鼠退行性骨关节病软骨细胞NF-κB信号通路的影响[J]. 中国老年学杂志,2017,37(13):3132-3134. DOI:10.3969/j.issn.1005-9202.2017.13.005.
[16] FAN XG,PEI SY,ZHOU D,et al. Melittin ameliorates inflammation in mouse acute liver failure via inhibition of PKM2-mediated Warburg effect[J]. Acta Pharmacol Sin,2021,42(8):1256-1266. DOI:10.1038/s41401-020-00516-0.
[17] WANG X,YU HJ,ZHANG YH,et al. Curcumin alleviates osteoarthritis through the p38MAPK pathway:network pharmacological prediction and experimental confirmation[J]. J Inflamm Res,2024,17:5039-5056. DOI:10.2147/JIR.S459867.
[18] FLORES-ROMERO H,HOHORST L,JOHN M,et al. BCL-2-family protein tBID can act as a BAX-like effector of apoptosis[J]. EMBO J,2021,41(2):e108690. DOI:10.15252/embj.2021108690.
[19] ZHU WC,YANG XH,LIU SJ,et al. Lentivirus-based shRNA of *Caspase-3* gene silencing inhibits chondrocyte apoptosis and delays the progression of surgically induced osteoarthritis[J]. Biotechnol J,2024,19:e2300031. DOI:10.1002/biot.202300031.
[20] SCANU A,LORENZIN M,LUISETTO R,et al. Identification in synovial fluid of a new potential pathogenic player in arthropathies[J]. Exp Biol Med,2022,247(12):1061-1066. DOI:10.1177/15353702221087966.
[21] SHIN Y,CHO D,KIM SK,et al. STING mediates experimental osteoarthritis and mechanical allodynia in mouse[J]. Arthritis Res Ther,2023,25(1):90. DOI:10.1186/s13075-023-03075-x.
[22] ZHENG JR,MA ZT,LIU P,et al. EZH2 inhibits senescence-associated inflammation and attenuates intervertebral disc degeneration by regulating the cGAS/STING pathway via H3K27me3[J]. Osteoarthr Cartil,2025,33(5):548-559. DOI:10.1016/j.joca.2025.02.771.

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tients with delayed encephalopathy after acute carbon monoxide poisoning[J]. Behav Neurol,2020,2020:1719360. DOI:10.1155/2020/1719360.
[13] 丛岩,王培,孙志德,等. 神经营养因子3通过激活自噬抑制焦亡促进脓毒症脑损伤后神经功能恢复[J]. 中国医科大学学报,2025,54(8):684-689. DOI:10.12007/j.issn.0258-4646.2025.08.003.
[14] LIU ZB,WANG LC,LIAN JJ,et al. Analysis of factors associated with the development of delayed encephalopathy following acute carbon monoxide poisoning[J]. Sci Rep,2024,14(1):14630. DOI:10.1038/s41598-024-64424-7.
[15] 朱红灿,岳培建. CO中毒迟发性脑病诊断与治疗中国专家共识[J]. 中国神经免疫学和神经病学杂志,2021,28(3):173-179. DOI:10.3969/j.issn.1006-2963.2021.03.001.
[16] WANG SD,FU YY,HAN XY,et al. Hyperbaric oxygen preconditioning protects against cerebral ischemia/reperfusion injury by inhibiting mitochondrial apoptosis and energy metabolism disturbance[J]. Neurochem Res,2021,46(4):866-877. DOI:10.1007/s11064-020-03219-4.
[17] 黄芳玲,黄艳青,黄旭,等. 高压氧对急性一氧化碳中毒迟发性脑病患者痴呆症状的影响[J]. 中南大学学报(医学版),2023,48(11):1669-1677. DOI:10.11817/j.issn.1672-7347.2023.230240.
[18] XIAO J,LI WJ,LI GJ,et al. STK11 overexpression prevents glucocorticoid-induced osteoporosis via activating the AMPK/SIRT1/PGC1α axis[J]. Hum Cell,2022,35(4):1045-1059. DOI:10.1007/s13577-022-00704-6.
[19] YANG XY,LI QJ,ZHANG WC,et al. AMPK-SIRT1-PGC1α signal pathway influences the cognitive function of aged rats in sevoflurane-induced anesthesia[J]. J Mol Neurosci,2020,70(12):2058-2067. DOI:10.1007/s12031-020-01612-w.
[20] ELESAWY WH,EL-SAHAR AE,SAYED RH,et al. Repurposing ezetimibe as a neuroprotective agent in a rotenone-induced Parkinson's disease model in rats:role of AMPK/SIRT-1/PGC-1α signaling and autophagy[J]. Int Immunopharmacol,2024,138:112640. DOI:10.1016/j.intimp.2024.112640.
[21] ZAHEDI E,SADR SS,SANAEIERAD A,et al. Valproate-induced murine autism spectrum disorder is associated with dysfunction of amygdala parvalbumin interneurons and downregulation of AMPK/SIRT1/PGC1α signaling[J]. Metab Brain Dis,2023,38(6):2093-2103. DOI:10.1007/s11011-023-01227-1.
[22] 胡滨,王大斌,郭茂. 川穹嗪调节SIRT1/AMPK/PGC1α信号通路对偏头痛大鼠镇痛作用及神经元损伤的影响[J]. 天津医药,2023,51(4):382-387. DOI:10.11958/20220873.

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