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锰卟啉络合物对MPTP诱导的帕金森病小鼠的防治作用

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陈平1 何斌2 艾自胜3 娄晓初1 李昂1 陈震4 吴晓康4 梁立平1*

1.同济大学生命科学与技术学院，上海 200092；2.同济大学电子信息学院，上海 200092；3.同济大学医学院预防医学教研室，上海 200092；4.同济大学附属上海市第十人民医院脑外科，上海 200072

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摘要：

目的：观察锰卟啉络合物\[manganese(III) meso-tetrakis(N,N′-diethylimidazolium-2-yl) porphyrin,MnTDM\]对1-甲基-4-苯基-1,2,3,6-四氢吡啶(1-methyl-4-phenyl-1,2,3,6- tetrahydropyridine，MPTP)诱导的早期帕金森病模型小鼠的防治效果，探讨其可能的作用机制。方法：C57BL/6雄性小鼠随机分为MPTP模型组（连续3 d皮下注射25 mg/kg MPTP），MnTDM+MPTP组（于MPTP注射前1 h皮下注射15 mg/kg MnTDM）以及MnTDM对照组、生理盐水对照组，每组10只。末次注射后第3日进行爬杆和游泳等行为学检测；HPLC-ECD法检测各组小鼠纹状体多巴胺(dopamine，DA)及其代谢产物3,4-二羟基苯乙酸（DOPAC）和高香草酸（HVA）水平；硫代巴比妥酸（thiobarbituric acid，TBA）法测定各组小鼠纹状体丙二醛(malondialdehyde，MDA)水平。结果：急性注射MPTP可建立早期帕金森病小鼠模型；与对照组相比，MPTP组小鼠纹状体DA、DOPAC、HVA水平明显下降（P<0.01），MDA水平明显升高（P<0.05）；但短期对小鼠行为学指标影响不大。MnTDM 能部分抑制MPTP的上述作用；与MPTP组相比，MnTDM+MPTP组小鼠纹状体DA、DOPAC、HVA水平明显上升，MDA水平明显下降（P均<0.05）。各组小鼠间行为学指标无统计学差异。结论：MnTDM能抑制脂质过氧化，促进多巴胺类神经递质分泌，对MPTP诱导的帕金森病小鼠有一定防治作用。

关键词：帕金森病 MPTP 锰卟啉络合物 氧化应激

Catalytic metalloporphyrin protects against MPTP-induced Parkinson's disease in mice

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CHEN Ping1 HE Bin2 AI Zi-sheng3 LOU Xiao-chu1 LI Ang1 CHEN Zhen4 WU Xiao-kang4 LIANG Li-ping1*

1.School of Life Science and Technology, Tongji University, Shanghai 200092, China; 2.School of Electronics and Information, Tongji University, Shanghai 200092; 3.Department of Preventive Medicine, School of Medicine, Tongji University, Shanghai 200092; 4.Department of Brain Surgery, the 10th People's Hospital of Shanghai, Tongji University, Shanghai 200072

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Abstract:

Objective:To observe the effects of manganese(III) meso-tetrakis(N, N′-diethylimidazolium-2-yl) porphyrin(MnTDM) in treatment of early Parkinson's disease(PD) mouse model induced by subcutaneous injection of 1-methyl-4-phenyl-1, 2, 3, 6-tetrahydropyridine(MPTP) and to discuss its possible mechanism. Methods:Forty male C57BL/6 mice were evenly randomized into 4 groups: MPTP model group(subcutaneous injection of 25 mg/kg MPTP for 3 days), MnTDM+MPTP group(15 mg/kg MnTDM was subcutaneously injected 1 h before MPTP injection), MnTDM control group, and normal saline group. Performance of animals in the pole and swimming test was observed 3 days after the last injection. Levels of dopamine(DA) and its metabolites(3,4-dihydroxyphenylacetic acid \[DOPAC\] and homovanillic acid \[HVA\]) in the striatum of animals were measured by high-performance liquid chromatography with an electrochemical detector(HPLC-ECD). Thiobarbituric acid(TBA) method was used to examine the levels of malondialdehyde(MDA). Results:Acute injection of MPTP could be used for establishment of PD model. The striatal levels of DA, DOPAC and HVA in MPTP group were significantly lower(P<0.01) and the striatal level of MDA was significantly higher(P<0.05) than those of the control group. MPTP had no obvious effect on the behavioral performance of the animals in a short term. MnTDM could partly inhibit the above effects of MPTP. Compared with MPTP group, MnTDM+MPTP group had significantly higher DA, DOPAC, and HVA levels and significantly lower MDA level(all P<0.05). There was no significant difference in the behavioral indices of animals between the 4 groups. Conclusion:MnTDM can inhibit lipid peroxidation and promote DA production;it has preventive and therapeutic effects on MPTP-induced PD.

Keywords: Parkinson disease MPTP MnTDM oxidative stress

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