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帕金森病模型小鼠黑质纹状体系统氧化应激的增龄性改变

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Impact of aging on the nigro-strital oxidative stress in a mice model of Parkinson's disease

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摘要/Abstract

摘要： 目的 观察不同月龄小鼠帕金森病（PD）模型黑质纹状体系统氧化应激损伤的增龄性改变并检测老龄PD小鼠氧化应激相关基因的差异性表达。**方法** 选用健康雌性3、6、10月龄快速老化小鼠P8系（SAMP8）42只，各月龄小鼠随机平均分为MPTP组与对照组，分别给予背部皮下急性注射1-甲基-4-苯基-1，2，3，6-四氢吡啶（MPTP）及等量0.9%NaCl处理。给药后72 h，采用开

放旷场实验观察其运动功能，高效液相色谱法检测黑质DA含量，分光光度计法检测纹状体超氧化物歧化酶（SOD1）活性和丙二醛（MDA）含量，比较不同月龄小鼠黑质DA系统、纹状体氧化应激相关指标损伤的差异。采用PCR Array检测两组10月龄小鼠纹状体氧化应激相关基因表达的差异。**结果** 与对照组相比，MPTP组各月龄小鼠水平运动距离与站立次数均减少，DA水平、SOD活性明显下降，MDA含量明显增加（P<0.05）；与3、6月龄相比，10月龄小鼠上述指标变化更明显；与对照组相比，10月龄MPTP组小鼠环氧化酶-2表达明显上调，而谷胱甘肽过氧化物酶3、6、8，乳酸过氧化物酶、核氧化还原酶、肌红蛋白、神经珠蛋白酶、过氧化物还原酶1和嗜酸粒细胞过氧化物酶9种基因明显下调（倍数改变>2）。**结论** 月龄是影响PD模型黑质纹状体系统损伤的重要因素；与氧化应激相关的基因的上调或下调可能参与了PD的早期发病。

关键词: 氧化应激, 帕金森病, 快速老化小鼠P8系, 增龄, 基因差异表达

Abstract: Objective To observe the age-related changes of nigro-strital oxidative stress in a mice model of Parkinson's disease(PD) at different ages and detect the differential expression of oxidative stress related genes in aged PD mice by using PCR Array. **Methods** Forty-two healthy female senescence-accelerated mouse prone 8 (SAMP8) mice aged 3, 6 and 10-month were averagely and randomly divided into 1-methyl-4-phenyl-1, 2, 3, 6-tetrahydropyridine (MPTP) group and control group, which were subcutaneously injected with MPTP or the same volum of 0.9% NaCl, respectively. After the first injection for 72 hours, behavioral changes in mice were examined by the open field test. The levels of dopamine (DA) in nigro-striatal system was measured by a high performance liquid chromatography with electochemical detector (HPLC-ECD). The activities of superoxide dismutase 1(SOD1) and the content of malondialdehyde(MDA) were detected by the spectrophotometer. The injuries of nigraldopamine system and striatal oxidative stress related indexes were compared among mice at different ages. The expression of striatal oxidative stress related gene expression in 10-month mice was detected by PCR Array. **Results** Compared with control group, the levels of DA andSOD 1, the performance in the open field test all decreased in MPTP group at three ages, while the content of MDA in tissue remarkably increased (P<0.01). Moreover, the above changes in 10-month mice were more obvious than 3- and 6-month mice (P<0.05). Compared with control group, the PCR Array results of MPTP group showed that COX-2 was up-regulated, while glutathione peroxidase 3, 6 and 8, lactoperoxidase, nucleoredoxin, myoglobin, neuroglobin, peroxiredoxin 1, eosinophil peroxidase were all down-regulated (fold change>2). **Conclusion** Aging plays an important role in nigro-striatal system injury of PD model. Up- or down- regulation of oxidative stress related genes may participate in the early phase of PD.

Key words: Oxidative stress, Gene differential expression, Parkinson's disease, Aging, Senescence-accelerated mouse prone 8

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