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论著

硫化氢通过抗氧化作用改善脑缺氧导致的小鼠空间记忆障碍

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摘要 **目的** 观察外源性H_2S对缺氧性脑损伤小鼠空间学习记忆障碍的影响，并探究其作用机制。**方法** 连续4 d sc给予$NaNO_2$ 120 mg·kg^{-1}·d^{-1}制备缺氧模型；氢硫化钠(NaHS)治疗组在制备模型的同时ip给予NaHS 1 mg·kg^{-1}·d^{-1}。每天给药前进行Morris水迷宫实验，测定逃避潜伏期、原平台象限停留时间和穿越平台次数。比色法检测小鼠脑组织中超氧化物歧化酶(SOD)活性及丙二醛(MDA)含量。HE染色观察海马组织切片CA1区神经元形态学改变。**结果** 水迷宫实验第3天和第4天，模型组小鼠逃避潜伏期分别为 (26.0±7.3)s和(23.3±8.7)s，明显长于正常对照组的(16.1±9.6)s(*P*<0.05)和(11.1±6.2)s(*P*<0.01)。第5天，模型组小鼠穿越平台次数为4.1±1.9，在原平台象限停留时间为(20±8)s，与正常对照组穿越平台次数(7.2±1.6)次和在原平台象限停留时间(28±8)s比较明显减少(*P*<0.01)。与正常对照组相比，模型组小鼠脑组织中SOD活性降低12.6%(*P*<0.01)，MDA含量升高43.9%（*P*<0.01)。在模型组小鼠海马CA1区，锥体细胞出现明显的核固缩、胞浆深染和排列紊乱等变性改变。与模型组比较，NaHS组小鼠在水迷宫实验的第3天和第4天逃避潜伏期明显缩短(*P*<0.05)，分别为(17.9±7.0)s和(15.8±8.5)s；在平台所在象限停留时间和穿越平台次数明显增加(*P*<0.01)，分别为(30±9)s和(6.7±2.5）次；SOD活性升高了8.9%(*P*<0.05)，MDA含量显著下降了29.6%(*P*<0.01)；海马CA1区神经元变性改变较模型组得到显著缓解。**结论** NaHS减轻了脑缺氧损伤诱发的小鼠学习记忆的损害，其作用机制可能与H_2S衰减海马区神经元损伤和抗氧化作用有关。

关键词 亚硝酸钠 硫化氢 学习记忆 神经元变性 海马 抗氧化作用

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Hydrogen sulfide attenuates spatial memory disorder induced by cerebral anoxia via antioxidation in mice

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Abstract

OBJECTIVE To investigate effects of exogenous hydrogen sulfide (H_2S) on the spatial memory disorder induced by cerebral anoxia in mice and explore related mechanism. **METHODS** Sodium nitrite ($NaNO_2$) 120 mg·kg^{-1} was sc given to mice for 4 d in model group. Sodium hydrosulfide (NaHS) 1 mg·kg^{-1} was ip given and $NaNO_2$ 120 mg·kg^{-1} simultaneously was sc given to mice for 4 d in NaHS group. All drugs were given to mice immediately after Morris water maze experiment every day and escape latency. The number of crossings over the target area (NCTA) and search time in target quadrant (STTQ) were recorded. The activity of superoxide dismutase(SOD) and malondialdehyde (MDA) level in the brain was determined with colorimetry. The morphological alterations in hippocampus slices were assessed by microscope. **RESULTS** On the third and fourth days in Morris water maze experiment, compared with (16.1±9.6)s and (11.1±6.2)s in normal control group, the escape latency in model group was longer, (26.0±7.3)s (*P*<0.05) and (23.3±8.7)s(*P*<0.01). On the fifth day, compared with 7.2±1.6 and (28±8)s in normal control group NCTA and STTQ in model group were 4.1±1.9 and (20±8)s (*P* <0.05), and they were obviously less. Compared with normal control group, SOD activity and MDA content of mice in model group were reduced by 12.6% (*P*<0.01) and increased by 43.9% (*P*<0.01), respectively. The neuron degenerative changes including karyopyknosis, dark cytoplasm and irregular pyramidal layer were observed in model group. On the third and fourth day, compared with model group, the escape latency in NaHS group was shorter, (17.9±7.0)s and (15.8±8.5)s (*P*<0.05). Compared with model group, NCTA and STTQ in NaHS group increased to 6.7±2.5 and (30±9)s (*P*<0.01). SOD activity and MDA content in NaHS group were increased by 8.9% (*P*<0.05) and reduced by 29.6% (*P*<0.01), respectively. Neuron degeneration was significantly attenuated in NaHS group (*P*<0.01). **CONCLUSION** NaHS can attenuate the spatial

memory disorder induced by cerebral anoxia and the mechanism may be related to the antioxidation effect and alleviation of neuron damage of H_2S.

Key words sodium nitrite hydrogen sulfide learning and memory neuron degeneration hippocampus antioxidation

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