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论著

脑内注射纳米三氧化二铁对大鼠空间学习记忆功能的影响及对腹侧中脑的损伤作用

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摘要 **目的** 探讨纳米三氧化二铁（nano-Fe_2O_3）对大鼠空间学习记忆功能的影响及其腹侧中脑的损伤作用。**方法** 立体定位下，大鼠中脑黑质和腹侧被盖区各一次性注射1 μl nano-Fe_2O_3 20 g·L^{-1}后，分别于1，2，3和4周组进行Morris水迷宫实验；取中脑行Perls反应法和免疫组织化学染色，观察多巴胺(DA)能神经元和胶质细胞的变化情况。**结果** 与正常对照组相比，脑内注射生理盐水对大鼠游泳速度、找到平台时间、潜伏期及搜索平台策略评分无影响。注射nano-Fe_2O_3后2和3周，大鼠找到平台时间和潜伏期明显延长（P<0.05）；正常对照组和溶剂对照组搜索平台策略以趋向式和随机式为主，注射nano-Fe_2O_3后各组均以趋向式和边缘式为主；各组游泳速度明显下降（P<0.05）。Perls反应和免疫组织化学染色结果显示，正常对照组与溶剂对照组均没有双标阳性细胞；nano-Fe_2O_3组药后1～4周均出现酪氨酸羟化酶(TH)/铁双标阳性细胞(TH$^+$/铁$^+$)、胶质体丝酸性蛋白质(GFAP)/铁双标阳性细胞(GFAP$^+$/铁$^+$)、OX-42/铁双标阳性细胞(OX-42$^+$/铁$^+$)，但各组间数量没有明显统计学差异。与正常对照组相比，溶剂对照组TH$^+$，GFAP$^+$，OX- 42$^+$单标细胞无显著差异；而nano-Fe_2O_3组黑质和腹侧被盖区均出现DA能神经元数量减少，少数DA能神经元胞浆内有nano-Fe_2O_3沉积，星形胶质细胞和小胶质细胞在注射区数目增加并且吞噬nano-Fe_2O_3颗粒。**结论** 脑内注射nano-Fe_2O_3能引起DA能神经元的破坏及胶质细胞数目和形态的改变，影响大鼠的空间学习记忆功能。

关键词 三氧化二铁纳米颗粒 学习 多巴胺能神经元 神经胶质 多巴胺

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Effect of intracerebral injection of ferric oxide nanoparticles on spatial learning and memory in rats and their injury to ventral midbrain

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Abstract

OBJECTIVE To explore the effect of ferric oxide nanoparticles (nano-Fe_2O_3) on the spatial learning and memory and their injury to the ventral midbrain in rats. **METHODS** One microliter nano-Fe_2O_3 20 g·L^{-1} was injected once respectively into the substantia nigra (SN) and ventral tegmental area (VTA) of the ventral midbrain by using the 3-dimensional positioning. The rats were divided into 1, 2, 3 and 4 week groups after the injection of 1 μl nano-Fe_2O_3 20 g·L^{-1} solution and were tested by Morris water maze respectively. Dopaminergic neurons and glial cells were observed by double staining of the Perls reaction and immunohistochemiscal reaction. **RESULTS** Compared with normal control group, rats in saline control group had no changes in the swimming speed, the time taken to find the platform, latency and the strategy of searching for the platform. Cmpared with normal control group, the swimming speed and the time taken to find the platform in nano-Fe_2O_3 2 and 3 week groups were prolonged significantly (P<0.05). The main modes strategy in normal control group and saline control group were the trend style and random style, but it was random style and edge style in nano-Fe_2O_3 groups. The swimming speed in nano-Fe_2O_3 groups decreased significantly (P<0.05). Double staining results showed that the normal control group and saline group did not have double-positive cells while nano-Fe_2O_3 groups had tyrosine hydroxylase positive (TH$^+$)/iron$^+$, GFAP$^+$/iron$^+$, OX-42$^+$/iron$^+$ double cells. The number of double cell had no statistical significance between each group. TH$^+$, GFAP$^+$, OX-42$^+$ single-labeled cells between saline group and normal group were not significantly different. Compared with normal control group, the number of dopaminergic neurons of nano-Fe_2O_3 groups was reduced in SN and VTA. A few of

dopaminergic neuron cytoplasms had the nano-Fe_2O_3 deposition. Astrocytes and microglia increased in the injection zone and could phagocytize iron nanoparticles. **CONCLUSION** Intracerebral injection of nano-Fe_2O_3 can cause damage to dopaminergic neurons, change the glial cell number and morphology, and affect spatial learning and memory in rats.

Key words ferric oxide nanoparticles learning neurons dopaminergic neuroglia dopamine

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