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隐性弓形虫感染小鼠的学习记忆能力障碍研究

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Impairment of Learning and Memory Ability in Mice with Latent Infection of *Toxoplasma gondii*

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摘要

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摘要 目的 应用物体识别试验和Morris水迷宫试验检测隐性弓形虫感染小鼠的学习记忆能力。方法 36只昆明小鼠随机分为对照组、低剂量弓形虫包裹感染组(低感染组)和高剂量弓形虫包裹感染组(高感染组),每组12只,低感染组和高感染组每鼠分别经口感染弓形虫Prugniaud (PRU)弱毒株6个和12个包裹。感染后第63天进行物体识别试验,通过第1天的适应期和第2天的熟悉期,于试验第3天记录小鼠对新旧不同物体的探究时间,计算分辨指数(DI)。感染后第66天进行Morris水迷宫试验,分别通过定位航行试验、空间搜索试验和工作记忆试验检测各组小鼠的空间记忆获得能力、空间记忆保持能力和工作记忆能力。于水迷宫试验结束当天,即感染后第74天处死小鼠,取左侧脑组织固定,切片,伊红?鄂苏木素染色后,镜下观察病理改变。右侧脑组织用于检测超氧化物歧化酶(SOD)活性和丙二醛(MDA)含量。结果 物体识别试验结果显示,高感染组和低感染组小鼠的分辨指数分别为(14.3±5.2)%和(17.5±5.6)%,均显著低于对照组[(28.9±7.1)%]($P<0.01$)。在定位航行试验中,两个弓形虫感染组小鼠找到平台的逃避潜伏期均长于对照组,其中试验第2天和第3天感染组和对照组间差异有统计学意义($P<0.05$)。在空间搜索试验中,高感染组和低感染组小鼠穿越原平台所在象限的距离占游泳总距离的(19.9±5.0)%和(23.9±6.8)%,与对照组[(27.4±3.6)%]比较差异有统计学意义($P<0.05$)。在工作记忆试验中,试验第4天高感染组和低感染组小鼠的逃避潜伏期[(36.5±14.2) s和(35.3±13.7) s]均比对照组[(30.4±12.5) s]显著延长($P<0.05$)。所有试验中,低感染组和高感染组小鼠各观察指标的差异均无统计学意义(均 $P>0.05$)。两组弓形虫感染小鼠的脑组织切片中均见弓形虫包裹,神经胶质细胞增生,小血管周围间隙增宽,出现“血管袖套”现象。高感染组和低感染组小鼠脑组织SOD活性均显著低于对照组,而MDA含量则均显著高于对照组(均 $P<0.05$)。2个感染组间差异无统计学意义($P>0.05$)。结论 隐性弓形虫感染可导致小鼠学习记忆能力障碍。

关键词: 刚地弓形虫 隐性感染 学习记忆 物体识别试验 Morris水迷宫试验

Abstract: Objective To detect the learning and memory ability in mice model of latent *Toxoplasma gondii* infection with object recognition test and Morris water maze test. Methods Thirty-six Kunming mice were divided into control group, infection group with 6 cysts each mouse (low infection group), and infection group with 12 cysts each mouse (high infection group) averagely. Mice in the two infection groups were orally infected with *T. gondii* Prugniaud (PRU) low virulence strain. Object recognition test was conducted at the 63rd day after infection. After the first day of adaptation and the second day of familiarization in the test, the time expended on exploring new and familiar objects was recorded on the third day and the discrimination index (DI) was calculated. Morris water maze test was conducted at the 66th day. The ability of spatial learning, spatial memory retention and working memory capacity was evaluated by place navigation test, spatial probe test, and working memory test, respectively. The mice were sacrificed at the 74th day after infection. The left cerebral hemisphere of mice was fixed, sliced, and stained with eosin-hema-toxylin for pathological examination. The right hemisphere was used to detect the activity of superoxide dismutase (SOD) and malondialdehyde (MDA) content. Results The results of object recognition test showed that the discrimination index of high infection group and low infection group was (14.3±5.2)% and (17.5±5.6)%, respectively, significantly lower than the control [(28.9±7.1)%] ($P<0.01$). In the place navigation test, the latency to find the platform in the two infection groups was longer than the control, with significant difference on the second and third day ($P<0.05$). In the spatial probe test, the percentage of the distance across the platform quadrant in the total swimming distance of high infection group and low infection group were (19.9±5.0)% and (23.9±6.8)%, respectively, significantly lower than the control [(27.4±3.6)%] ($P<0.05$). In the working memory test, at the fourth day of test the latency of high infection group and low infection group [(36.5±14.2) s and (35.3±13.7) s] was significantly longer than the control [(30.4±12.5) s] ($P<0.05$). In all the tests, there was no statistical significance between low infection group and high infection group ($P>0.05$). The brain sections of two infection groups showed cysts of *T. gondii*, proliferation of glial cells, widened gap around small blood vessels, and a phenomenon of “vascular cuff”. The activity

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SOD in the mice brains of two infection groups was significantly lower than the control, while MDA level was significantly higher ($P<0.05$). SOD and MDA showed no significant difference between two infection groups ($P>0.05$). Conclusion Latent infection of *T. gondii* may lead to learning and memory impairment in mice.

Keywords: *Toxoplasma gondii* Latent infection Learning and memory Object recognition test Morris water maze test

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