

274-276

# 海马注射缩宫素对大鼠穿梭箱回避行为的影响

周毓生<sup>1</sup>、张长城 (第三军医大学生理教研室, 重庆 630038, 中国)

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Effect of hippocampal injection of oxytocin on shuttle-box avoidance behavior of rats

## MATERIALS AND METHODS

ZHOU Yu-Sheng<sup>1</sup>, ZHANG Chang-Cheng  
(Department of Physiology, Third Military Medical College, Chongqing 630038, China)

**套管埋植** Wistar 大鼠 45 只, 雌雄不拘, 体重  $203 \pm s 27$  g, 3% 戊巴比妥钠  $30 \text{ mg} \cdot \text{kg}^{-1}$  ip 麻醉, 固定于脑立体定位仪上, 按照 Bures 大鼠脑定位图谱<sup>(8)P 3.0, LR 1.4, H 3.5</sup>, 将 8 号注射针头制成的套管埋植于背侧海马(双侧), 并用牙托粉固定于颅骨上, 以  $4\frac{1}{2}$  号针头充当注射管, 其下端突出套管 0.1 mm, 上端经塑料管与微量进样器连接. 术后恢复 5 d. 实验结束后, 经套管注入 2% pontamine sky blue, 核对定位.

**ABSTRACT** Bilateral dorsal hippocampal injection of oxytocin (Oxy, 50  $\mu\text{g}$ , on each side) in rats impaired the acquisition of conditioned avoidance behavior and accelerated the extinction of conditioned avoidance behavior in shuttle-box. The data suggested that the effect of Oxy on shuttle-box conditioned avoidance behavior of rats was at least partly accomplished via the hippocampus; Oxy affected short-term memory as well as long-term memory.

**行为实验** 穿梭箱(shuttle-box)  $50 \text{ cm} \times 20 \text{ cm} \times 30 \text{ cm}$ , 分成两室, 有  $6 \text{ cm} \times 8 \text{ cm}$  的拱形小门相通. 室底铜栅可通交流电(25 V, 0.3 mA, 50 Hz)作为非条件刺激(unconditioned stimulus, US). 两室侧壁各装一小灯泡(3 W), 以灯光为条件刺激(conditioned stimulus, CS). 将大鼠放入箱内适应 5 min. 给予 CS, 持续 15 s, 后 10 s 同时给予 US, 大鼠受电击后逃至另一室. 15 s 后, 另一室按同法进行. 每日训练 50 次, 使大鼠形成条件回避反应(conditioned avoidance response, CAR).

**KEY WORDS** hippocampus; oxytocin; avoidance learning; memory

**提要** 大鼠两侧背海马各注射缩宫素 50  $\mu\text{g}$  损害大鼠穿梭箱条件回避行为的习得, 并加速大鼠穿梭箱条件回避行为的消退. 结果提示, 缩宫素对穿梭箱条件回避行为的影响, 至少部分通过海马起作用; 缩宫素不仅对长时记忆而且对短时记忆亦有阻碍作用.

**关键词** 海马; 缩宫素; 回避学习; 记忆 回避行为  
穿梭箱

由下丘脑的神经细胞所分泌的缩宫素(oxytocin, Oxy)与学习记忆的关系已有不少研究<sup>(1-3)</sup>. 临床观察表明 Oxy 对记忆具有阻碍作用<sup>(4,5)</sup>. Oxy 对记忆过程的影响可能与海马结构有关<sup>(6,7)</sup>, 但局部注射 Oxy 于海马, 对大鼠穿梭箱条件回避行为的影响却未见报道. 本工作旨在探讨海马内注射 Oxy 穿梭箱回避行为中的作用.

**药物** Oxy (美国 Sigma 公司产品)  $50 \text{ } \mu\text{g} \cdot \mu\text{l}^{-1}$  盐水(NS), 内含 HCl  $0.01 \text{ mol} \cdot \text{L}^{-1}$ . 每侧背海马各注射 50  $\mu\text{g}$ . 对照组给予等容量溶剂. 给药时, 以微量进样器恒速推注 2 min.

用组间 *t* 检验处理实验结果.

## RESULTS

**Oxy 对 CAR 习得的影响** 每日训练前给药组和对照组分别给予 Oxy 或 NS, 观察

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<sup>1</sup> Now in Department of Physiology, Guangzhou Military Health School, Guangzhou 510315, China

8 d. 结果显示, 于 d 3-7, 给药组 CAR 的出现率明显低于对照组, 其中以 d 5 差异最显著 (Fig 1).

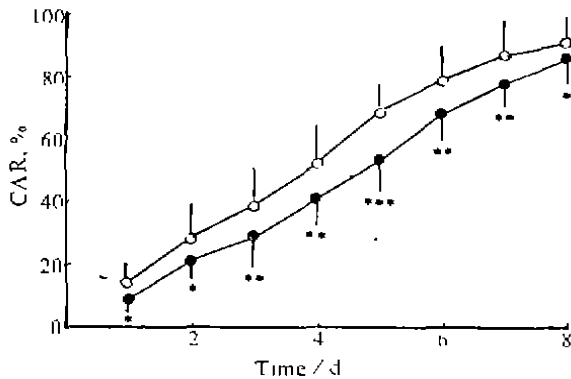


Fig 1. Effect of daily injection of Oxy (50 pg on each side) into bilateral dorsal hippocampus on acquisition of shuttle-box conditioned avoidance response (CAR) of rats. Control (○, n=13), Oxy (●, n=9).  $\bar{x} \pm s$ . \* $P > 0.05$ , \*\* $P < 0.05$ , \*\*\* $P < 0.01$ .

**Oxy 对 CAR 消退的影响** 训练前不给药物, 当大鼠 CAR 连续 3 d 达 80% 以上后, 立即给予 Oxy 或 NS, 给药后 24 h 和 48 h 检查大鼠 CAR 的保持情况. 结果见 Fig 2, 无论是 24 h 或 48 h, 给药组 CAR 的消退均较对照组快, 差异极为显著 ( $P < 0.01$ ).

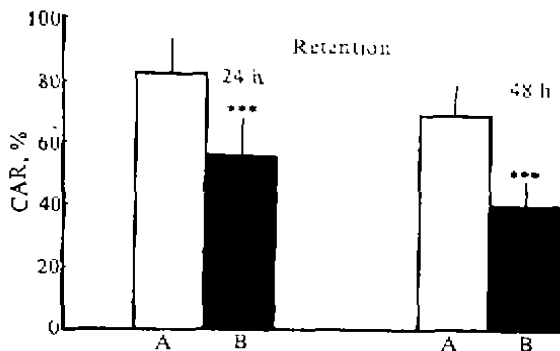


Fig 2. Effect of postlearning injection of Oxy into dorsal hippocampus bilaterally (50 pg on each side) on CAR of rats. (A) Control (n=11), (B) Oxy (n=12).  $\bar{x} \pm s$ . \*\*\* $P < 0.01$  vs control.

## DISCUSSION

不少实验表明, Oxy 对学习记忆的影响可能通过中枢起作用<sup>(9-11)</sup>, 而且可能与海马有关<sup>(6,7)</sup>. 本工作观察到, 海马注射 Oxy 对大鼠的学习记忆有明显的阻碍作用, 与文献的结果<sup>(6,7)</sup>相近. 此外, 由于每侧海马仅注射 Oxy 50 pg, 因此有可能完全或几乎完全在海马内发挥效应, 而不像从外周或脑室注射那样, 可通过血液或脑脊液作用于其它脑区. 由此提示, Oxy 对大鼠穿梭箱条件回避行为的影响, 很可能与海马有关, 至少部分通过海马起作用.

一般认为, Oxy 主要对记忆的巩固和恢复过程<sup>(6,12)</sup>即长时记忆产生影响, 而对动物行为的习得即短时记忆的作用却不甚明了, 尤其是对穿梭箱条件回避行为习得的效应如何仍未见报道. 本结果是, Oxy 不仅加速大鼠条件回避行为的消退, 而且还阻碍大鼠条件回避行为的习得. 由此提示, Oxy 对动物的长时记忆和短时记忆均有阻碍作用.

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276-279

### 4-(4''-(2'',2'',6'',6''-四甲基哌啶氮氧自由基)氨基)-4'-去甲基表鬼臼毒对 L7712 细胞的核酸、蛋白质及 DNA 链的影响

何小庆<sup>1</sup>, 张培棧, 田 瑄<sup>2</sup>, 李景新<sup>2</sup> R963

(兰州医学院药理教研室, <sup>2</sup>兰州大学应用有机化学实验室, 兰州 730000, 中国)

**Effects of 4-(4''-(2'',2'',6'',6''-tetramethyl-1''-piperidinyloxy)amino)-4'-demethylepipodophyllotoxin on nucleic acids, proteins, and DNA strand of L7712 cells in vitro**

HE Xiao-Qing<sup>1</sup>, ZHANG Pei-Yan, TIAN Xuan<sup>2</sup>, LI Jin-Xin<sup>2</sup>

(Department of Pharmacology, Lanzhou Medical College; <sup>2</sup>Applied Organic Chemistry Laboratory, Lanzhou University, Lanzhou 730000, China)

**ABSTRACT** The antitumor activity of GP-7, a new spin-labeled epipodophyllotoxin, was studied by liquid scintillation spectrometry. There were many similarities between GP-7 and etoposide. Both GP-7

and etoposide inhibited the incorporation of [<sup>3</sup>H]TdR, [<sup>3</sup>H]UR, and [<sup>3</sup>H]Leu into DNA, RNA, and protein synthesis in leukemia 7712 cells. The inhibition correlated with drug concentration and duration. IC<sub>50</sub> of GP-7 and etoposide on DNA synthesis at 24 h were 0.21 and 0.37 μg · ml<sup>-1</sup>, respectively. The inhibition of GP-7 or etoposide on DNA synthesis retained even after the drug were washed out for 3 h. GP-7 and etoposide caused DNA single-strand breaks, with a well concentration-response relationship. These data suggest that the inhibition of DNA synthesis by GP-7 or etoposide is likely due to the damage of DNA template and breaking of single-strand DNA.

**KEY WORDS** podophyllotoxin; free radicals; leukemia L7712; thymidine; uridine; leucine; single-stranded DNA; etoposide

**提要** 用液体闪烁计数法对 GP-7 的抗肿瘤作用进行

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<sup>1</sup> Now in Institute of Materia Medica, Chinese Academy of Medical Sciences, Beijing 100050, China.