部位之一. 酞菁类化合物性质稳定，对红光有强吸收，而 HpD 最大光吸收在 400 nm 左右，临床治疗是红光照射，所以酞菁类能够发挥其最大光敏效力. 从我们和他人对酞菁类光敏剂的研究结果，提示它是一类较好的光敏剂，有希望成为临床有用的光敏药物.

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# 苯环利定对离体兔脑基底动脉和整体脑血流的作用

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**Effects of phencyclidine on rabbit basilar artery *in vitro* and rabbit cerebral blood flow *in vivo***

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**ABSTRACT** The effect of phencyclidine [1-(1-phenylcyclohexyl)piperidine, PCP] on rabbit basilar arteries was studied with an *in vitro* model of ring segment arteries. PCP 0.05-500 $\mu mol \cdot L^{-1}$ caused vasoconstriction of basilar arteries in a concentration-dependent manner. Its maximal effect ($E_{max}$) was 94 ± 21 mg and the concentration causing half maximal effect ($EC_{50}$) was 25 ± 18 $\mu mol \cdot L^{-1}$. PCP 0.01-10 $\mu mol \cdot L^{-1}$ also concentration-dependently augmented the vasoconstriction induced by electric stimulation in rabbit basilar arteries. Its $E_{max}$ was 91 ± 18 mg and $EC_{50}$ was 0.27 ± 0.17 $\mu mol \cdot L^{-1}$.

The effects of PCP on mean arterial blood pressure (MABP) and heart rate (HR) of rabbits were observed. PCP iv 4 $mg \cdot kg^{-1}$ reduced MABP from 14.3 ± 0.8 to 12.2 ± 1.0 kPa and HR from 300 ± 0 to 278 ± 5 bpm in 5 min.

Using the technique of radionuclide imaging in rabbit brain *in vivo*, we studied the effect of PCP on

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cerebral blood flow. After iv PCP 4 mg · kg$^{-1}$, the $t_p$ of radiocerebrogram was increased from 4.5± 1.1 to 6.1± 1.0 s, the $t_g$ of radiocerebrogram was increased from 11.7± 0.6 to 18.2± 3.3 s and the rate of clearance was decreased. After iv PCP 2 mg · kg$^{-1}$, only $t_g$ increased from 12.6± 2.1 to 15.9± 0.6 s. Hence PCP increased the transit time of nondiffusible indicators ($^{99m}$Tc) through the cerebral circulation.

These results suggest that PCP causes constriction of basilar artery and slows down the cerebral blood flow.

**KEY WORDS** phencyclidine; basilar artery; radionuclide imaging; brain; blood flow velocity

**提要** 用离体血管环肌张力试验和脑放射图技术研究了苯环利定[1-(1-phenylcyclohexyl)piperidine, PCP]对兔脑基底动脉和脑血流的作用. PCP 能呈浓度依赖地引起兔脑基底动脉收缩，也能加强电场刺激引起兔脑基底动脉收缩. iv PCP 能延长放射性核素脑内通过时间，降低血液清除率. 提示 PCP 可能通过收缩脑血管使脑血流速度减缓.

**关键词** 苯环利定；基底动脉；放射性核素成象；脑；血流速度

苯环利定[1-(1-phenylcyclohexyl) piperidine, PCP] 类药物非竞争性地拮抗了兴奋性氨基酸 NMDA 受体的功能[1,2]，对实验性脑缺血动物有神经保护作用[3-5]. 我们曾报道脑血管上有 PCP 受体[6,7]. PCP 能引起离体猪脑血管灌流压升高[6]. 本文观察了 PCP 对离体兔脑基底动脉和整体兔脑血流的作用，为研究 PCP 类药物保护缺血性脑损伤的作用机制，从其具有脑血管生物活性这一角度提供新的思路.

## MATERIALS AND METHODS

新西兰兔 34 只，♀♂兼用，体重 2.7± SD 0.3 kg，由本校实验动物部提供.

PCP 由本校药学院合成；$^{99m}TcO_4^-$ (890 EBq · mol$^{-1}$)为钠盐，法国 CIS 公司产品；亚锡植酸钠，本校红旗药厂产品.

**兔基底动脉环肌张力试验** 取兔脑基底动脉长约 4-5 mm，浸入克氏液中. 在血管腔内穿入两根直径为 0.3 mm 的不锈钢丝，其中一根固定在电极板上，另一根用线连结到张力换能器上. 将电极板置入 4 ml 浴槽中，37± 0.5℃，通 95% $O_2$ + 5% $CO_2$. 标本负荷为 0.5 g. 平衡 3-4 h 后给予药物或电刺激(15-30 V, 0.8 ms, 8 Hz 和 50 pulses; 刺激间隔为 5 min). 观察血管的收缩反应. 药物作用强度以肌张力的增加表示. 用 Scott 公式计算 $EC_{50}$ 和 $E_{max}$.

**血压和心率测定** 兔，iv 1.5%戊巴比妥钠(2 ml · kg$^{-1}$)麻醉. 分离一侧股动脉，插管连结压力换能器，再接 SJ-42 型多道生理记录仪，记录平均动脉血压(MABP)和心率(HR).

**脑放射血流图** 参照人脑放射血流图技术[8]操作. 兔经戊巴比妥钠麻醉. 取卧位，头部固定，颅顶对准探头面中心，颈部及以下部位铅板隔离. 耳缘静脉"弹丸"式注入 $^{99m}TcO_4^-$ 标记的亚锡植酸钠 79± 25 MBq (容量 0.2 ml 内). 注射同步，以每秒 1 帧，用单光子发射计算机断层扫描仪(SPECT)采集 64 帧图象信息. 30 min 后，iv PCP 2 or 4 mg · kg$^{-1}$ 或等体积 NS (1 ml · kg$^{-1}$). 待 30 min 后再以同样放射性同位素剂量再次采集 64 帧图象信息.

**图象及数据处理** 用脑血流图程序，将大脑左右半球框为一个感兴趣区. 经计算机处理，显示大脑血流曲线，从曲线起始到顶峰时间($t_p$)反映了放射性核素由颈内动脉向大脑前、中动脉及其主要分支灌流的过程. 峰顶至降支终点的时间($t_g$)反映了核素由微血管经脑静脉系统排出的过程. 顶峰后曲线下降情况也代表了放射性核素脑血液清除情况.

## RESULTS

**PCP 对离体兔脑基底动脉的作用** PCP 能引起兔脑基底动脉收缩. 随着 PCP 浓度增大，其作用不断增强. 在 PCP 的浓度以 10 倍的等比级数从 0.05-500 μmol · L$^{-1}$ 增加时，

效应呈浓度依赖关系(Fig 1). 当 PCP 的用量为 1000 μmol · $L^{-1}$ 时，药物作用强度略有减弱. 最大效应($E_{max}$)为 94 ± 21 mg，半数有效浓度($EC_{50}$)为 25 ± 18 μmol · $L^{-1}$.

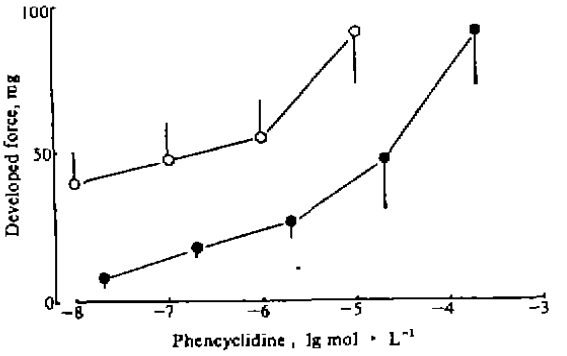


**Fig 1. Effects of phencyclidine on electrical stimulation-induced contraction (○, $n=5$) and on isometric tension (●, $n=3$) in rabbit basilar arteries. $\bar{x}\pm$ SD.**

PCP 的浓度以 10 倍的等比级数从 0.01~10 μmol · $L^{-1}$ 增加时，也能呈浓度依赖地加强电刺激引起兔脑基底动脉收缩的作用(Fig 1). PCP 的浓度大于 10 μmol · $L^{-1}$ 时，其加强电刺激引起血管收缩的作用小于 PCP 浓度为 10 μmol · $L^{-1}$ 时的作用. 其 $E_{max}$ 为 91 ± 18 mg，$EC_{50}$ 为 0.27 ± 0.17 μmol · $L^{-1}$.

**PCP 对兔 MABP 和 HR 的作用** iv PCP 后兔 MABP 和 HR 均呈下降趋势，但 PCP 1 or 2 mg · $kg^{-1}$ 降低 MABP 和 HR 的作用与给药前比，差别均无显著性. iv PCP 4 mg · $kg^{-1}$ 后 5 min 作用最强. MABP 由 14.3 ± 0.8 kPa 下降至 12.2 ± 1.0 kPa ($P<0.05$). HR 也由 300 ± 0 bpm 降至 278 ± 5 bpm ($P<0.05$). 15 min 后逐渐恢复(Fig 2).

**PCP 对整体兔脑血流的作用** iv PCP 2 mg · $kg^{-1}$ 后兔脑放射图上升段与给药前基本一致，$t_g$ 延长，清除能力下降. iv PCP 4 mg · $kg^{-1}$ 后兔脑放射图不仅 $t_g$ 延长，$t_p$ 也延长，

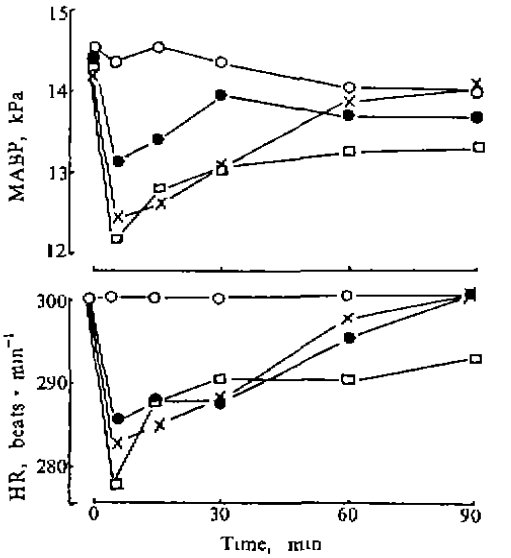


**Fig 2. Effects of phencyclidine on mean arterial blood pressure (MABP) and heart rate (HR) in rabbits. Saline (○), PCP 1 (●), 2 (×), 4 (□) mg · $kg^{-1}$. $n=4$, $\bar{x}\pm$ SD.**

清除能力进一步下降. 对照组给予 NS 前后，其脑放射图无明显变化. 见 Fig 3, Tab 1.

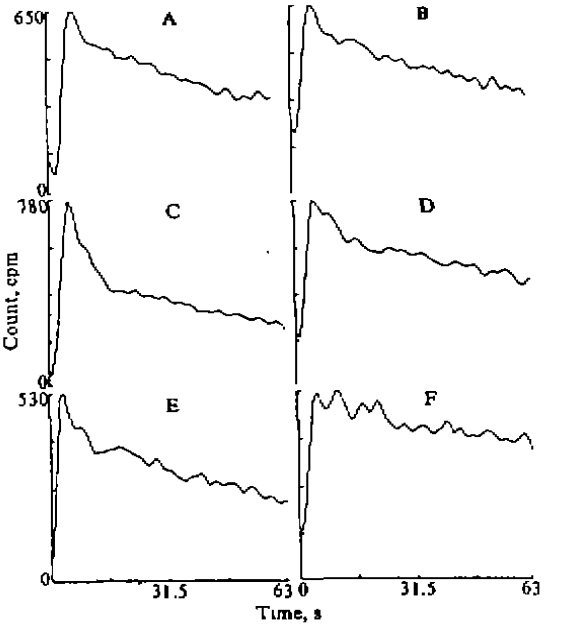


**Fig 3. Effects of phencyclidine on radiocerebrogram of rabbit. A & B: Saline; C & D: iv PCP 2 mg · $kg^{-1}$; E & F: iv PCP 4 mg · $kg^{-1}$. A, C, E: control; B, D, F: drug.**

**Tab 1. Effects of iv phencyclidine (PCP) on peak time ($t_p$) and gorge time ($t_g$) of rabbit radiocerebrogram. $\bar{x} \pm SD$. $^{*}P>0.05$, $^{**}P<0.05$, $^{***}P<0.01$ *vs* before PCP.**

| | NS | PCP 2 mg·kg$^{-1}$ | PCP 4 mg·kg$^{-1}$ |
|---|---|---|---|
| *n* | 4 | 3 | 3 |
| $t_p$, s | | | |
| before | 4.6±0.5 | 4.3±0.1 | 4.5±1.1 |
| after | 4.6±0.5$^{*}$ | 4.3±0.1$^{*}$ | 6.1±1.0$^{**}$ |
| $t_g$, s | | | |
| before | 11.3±1.6 | 12.6±2.1 | 11.7±0.6 |
| after | 12.0±2.5$^{*}$ | 15.9±0.6$^{**}$ | 18.2±3.3$^{***}$ |

## DISCUSSION

脑放射血流图实验结果表明 PCP 能使放射性核素脑内通过时间延长；脑的微血管系统和静脉系统对 PCP 的作用较大脑前、中动脉敏感.

虽然 PCP 的作用有种属差异性[9,11]，但是本实验发现 PCP 引起兔脑基底动脉收缩的作用与离体猪脑血管上的实验结果[6]一致.

系统给予 PCP 对血压和心率的影响较为复杂，有兴奋作用，也有抑制作用，抑或同时存在[9,11]. 本实验表明 PCP 1–4 mg·kg$^{-1}$ 对血压和心率的作用较弱，作用时间也短暂(仅 iv PCP 4 mg·kg$^{-1}$ 后 5 min 有作用). 因此我们认为本实验中 PCP 对心血管系统的作用对中枢血流量无明显影响. PCP 使放射性核素脑内通过时间延长的作用机制可能是通过直接收缩脑血管，增加血管阻力而减缓了脑血流速度.

脑放射血流图在反映脑血流动力学方面具有独特的灵敏性[8]. 虽然该方法仍属于半定量指标，影响因素较多，但本实验表明脑放射血流图结合其它药理学方法能够反映药物对脑血管和脑血流的作用.

脑血管上有 PCP 受体[6,7]，PCP 能收缩脑血管，减慢脑血流. 那么 PCP 对脑血管的作用在应用 PCP 类药物进行抗脑缺血性损伤的研究中具有怎样的意义？此项工作正在研究中.

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