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中国药理学报 *Acta Pharmacologica Sinica* 1990 Mar; 11 (2) : 130-133

麻黄碱对离体豚鼠门静脉突触后 α -受体和突触前 β -受体的作用¹

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Effects of ephedrine on postsynaptic α -adrenoceptors and presynaptic β -adrenoceptors in isolated guinea pig portal veins

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ABSTRACT. The effects of ephedrine (Eph) were compared with those of tyramine (Tyr)

and phenylephrine (Phe) in ring segments of guinea pig portal vein *in vitro*. Eph (3-1000 $\mu\text{mol/L}$), Tyr (10-1000 $\mu\text{mol/L}$) and Phe (1-1000 $\mu\text{mol/L}$) all produced concentration-dependent contractile responses, which were exceedingly depressed by α -adrenoceptor blocker phentolamine (31 $\mu\text{mol/L}$). Pretreatment with reserpine 1 mg/(kg·d) \times 2 d markedly diminished the effect of Tyr, but greatly potentiated the effects of Eph and Phe. Both Eph (1-30 $\mu\text{mol/L}$) and Tyr (10-100 $\mu\text{mol/L}$), but not Phe, significantly increased the electrical field stimulation (duration 2 ms, 3 Hz, 10 s, 50 V, 10 min intervals) evoked contractions of the portal veins. β -Adrenoceptor blocker propranolol (0.5 $\mu\text{mol/L}$) greatly inhibited this effect of Eph, without affecting that of Tyr. It is suggested that the effect of Tyr is mainly due to its release of endogenous norepinephrine (NE) from the nerve terminals; conversely, Eph mainly acts on postsynaptic α -adrenoceptors directly with some NE-releasing action which may involve the activation of presynaptic β -adrenoceptors.

KEY WORDS ephedrine; portal vein; alpha

Received 1989 Feb 2 Accepted 1989 Sep 1

¹ Project supported by the Science Fund of the Chinese Academy of Sciences, No Bio-365 and presented at the 5th Southeast Asian and Western Pacific Regional Meeting of Pharmacologists, Beijing, 1988 Jul 4-8.

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adrenergic receptors: electric stimulation; beta adrenergic receptors.

摘要 酚妥拉明抑制 Eph, Tyr 和 Phe 对豚鼠门静脉环的收缩作用, 而利血平处理后 Eph 和 Phe 的作用增强, Tyr 则减弱。Eph 和 Tyr 也增加电场刺激所致收缩, 而 Phe 则不能。普萘洛尔减弱 Eph 这一作用, 但不影响 Tyr 的作用。提示 Eph 的作用接近 Phe, 以直接激动突触后 α -受体为主, 但也具促进 NE 释放的间接作用, 后者与激动突触前 β -受体有关。

关键词 麻黄碱; 门静脉; α -肾上腺素受体; 电刺激; β -肾上腺素受体

已知麻黄碱(ephedrine, Eph)在心房⁽¹⁾以间接作用为主, 在动脉⁽¹⁾和输精管⁽²⁾以直接作用为主; 其对动脉和输精管的直接作用与激动 α_1 肾上腺素受体有关。而对心脏和气管⁽³⁾的直接作用与激动 β 受体有关。此外, Eph 尚可作用于输精管和回肠⁽⁴⁾的突触前 α_2 受体。放射性配体结合实验显示 Eph 在肺细胞膜制备能竞争 [³H]二氢烯丙洛尔的特异性结合⁽⁵⁾, 但其对静脉的作用却未见报道。本文目的为探讨 Eph 对豚鼠门静脉的直接和间接作用以及对肾上腺素受体的作用; 并与典型的间接作用拟交感胺, 酪胺(Tyramine, Tyr)和直接作用的去氧肾上腺素(phenylephrine, Phe)比较。

MATERIALS AND METHODS

麻黄碱(ephedrine)内蒙古赤峰制药厂产品; 酪胺(tyramine, Tyr) Sigma 产品; 去氧肾上腺素(phenylephrine, Phe)上海药检所赠; 普萘洛尔(propranolol)上海黄河制药厂产品; 酚妥拉明(phentolamine)上海第十三制药厂产品; 利血平(reserpine)上海医科大学红旗制药厂产品。

离体豚鼠门静脉环的制备 用体重 $351 \pm SD 29$ g 的 ♀ ♂ 豚鼠, 制备门静脉环⁽⁶⁾, 长约 4 mm, 水平悬挂于 37°C 的 Krebs-Henseleit 液中, 通以含 95% O_2 + 5% CO_2 的混合气体。调节静止张力 2 g, 稳定 1 h 后通过自制的张力换能器和平衡记录仪(XWC-300, 上海自

动化仪表二厂)描记门静脉的收缩。采用累积浓度法加入所试药物, 建立累积浓度-效应曲线(CCRC)。由于 Eph 和 Tyr 的作用有增敏现象, 在同一标本连续作的两条 CCRC 间有差异, 故采取组间比较, 以对照组的第 2 条 CCRC 与给药组加入阻断剂后的第 2 条 CCRC 进行比较。以对照组第 1 条 CCRC 0.3 mmol/L 的收缩为 100% 作图。

利血平处理 实验前 48 和 24 h 各给豚鼠 ip 利血平(1 mg/kg)一次。

电场刺激 按上述, 取约 4 mm 长一段豚鼠门静脉环, 悬挂于两个 L 下平行的铂电极之间, 进行电场刺激(波宽 2 ms, 3 Hz, 10 s, 50 V, 10 min 一次)。首先刺激 6 次, 待收缩幅度的变化小于 10% 时, 以第 6 次刺激所致收缩为对照 100%, 然后在对照刺激后的每次刺激前 1 min 加入药物, 一个标本共试 5-6 个药物浓度, 记录电场刺激所致收缩幅度的相对变化, 建立 CCRC。阻断剂一般在对照刺激前 20 min 加入。

实验结果采用配对数据 t 检验或两组数据 t 检验。

RESULTS

对静息张力的影响 Eph (3-1000 $\mu\text{mol/L}$), Tyr (10-1000 $\mu\text{mol/L}$) 和 Phe (1-1000 $\mu\text{mol/L}$) 都能使门静脉环产生浓度依赖性收缩, EC_{50} 分别为 70.8 ± 6.3 , 56.0 ± 4.3 和 $4.7 \pm 0.4 \mu\text{mol/L}$ 。加入酚妥拉明(31 $\mu\text{mol/L}$) 30 min 后, 其本身对门静脉张力无影响, 但可基本取消 3 种药的作用(Fig 1)。豚鼠用利血平处理后, Tyr 对门静脉的作用减弱(10 和 30 $\mu\text{mol/L}$ 时有显著性), 但没有被取消(尤其在高浓度), 而 Eph 的作用则明显增强, Phe 的作用也有所增加(Fig 1)。

对电场刺激所致收缩的影响 电场刺激能使门静脉产生位相性收缩, 河豚毒素(0.3 $\mu\text{mol/L}$) 和酚妥拉明(31 $\mu\text{mol/L}$) 几乎能完全阻断这种收缩, 说明电场刺激是兴奋神经末梢释放递

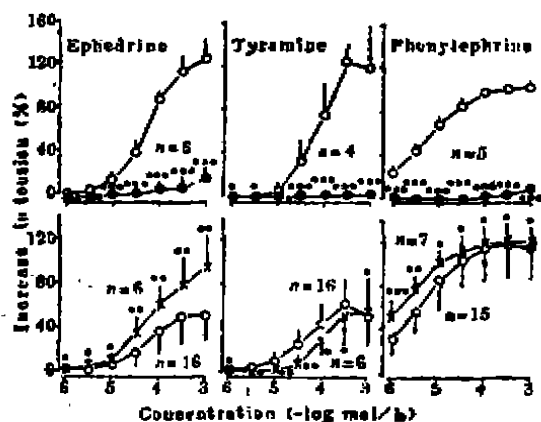


Fig 1. Effects of phentolamine and reserpine on the contractile responses of ephedrine (Eph), tyramine (Tyr) and phenylephrine (Phe) in isolated guinea pig portal veins, $\bar{x} \pm SD$, * $P > 0.05$, ** $P < 0.05$, *** $P < 0.01$. (○) Control, (●) Phentolamine 31 $\mu\text{mol/L}$ pretreated, (×) Reserpine 1 mg/(kg·d) $\times 2$ d pretreated.

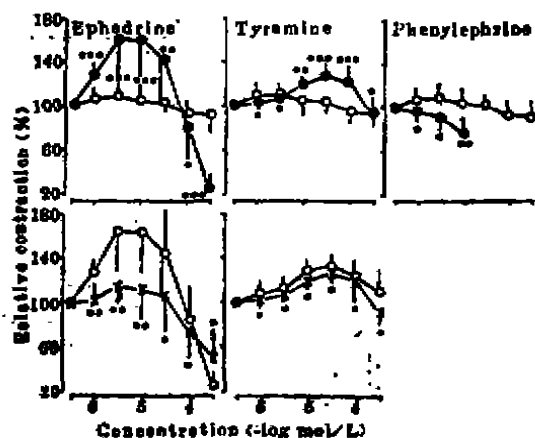


Fig 2. Effects of ephedrine (Eph), tyramine (Tyr) and phenylephrine (Phe) on the electrical field stimulation induced contraction in isolated guinea pig portal veins and the influence of propranolol, $\bar{x} \pm SD$, * $P > 0.05$, ** $P < 0.05$, *** $P < 0.01$. (○) Control ($n=6$) (●) Eph, Tyr or Phe ($n=5$), (×) Propranolol pretreated (0.5 $\mu\text{mol/L}$, $n=4$).

质去甲肾上腺素(norepinephrine, NE)引起收缩的。Eph(1-30 $\mu\text{mol/L}$)和 Tyr(10-100 $\mu\text{mol/L}$)均能增加电场刺激所致门静脉的收缩幅度, 高浓度 Eph(>0.3 mmol/L)则有明显抑制作用(Fig 2)。普萘洛尔(0.5 $\mu\text{mol/L}$)可明显抑制

Eph的作用, 对 Tyr影响不大(Fig 2)。低浓度 Phe(1和3 $\mu\text{mol/L}$)不影响电场刺激引起的收缩, 而较高浓度时(>10 $\mu\text{mol/L}$)则有抑制作用(Fig 2)。

DISCUSSION

本工作发现, Eph, Tyr和Phe都能使豚鼠门静脉环产生浓度依赖性收缩, 且都能为 α -受体阻断剂酚妥拉明所阻断(Fig 1), 说明它们直接作用于 α -受体或通过释放的递质 NE间接作用于 α -受体。利血平处理后, Eph和Phe对门静脉的收缩作用明显增强, 而Tyr的作用则减弱(Fig 1)。利血平能耗竭去甲肾上腺素能神经末梢的递质 NE, 利血平耗竭 NE后 Tyr作用明显减弱, 可见其主要通过释放的 NE间接作用于 α -受体, 但高浓度 Tyr的作用可能是其直接激活 α -受体所致; Tyr对兔耳动脉⁽⁸⁾、大鼠输精管⁽⁹⁾和豚鼠肺动脉等有类似的作用。Eph在利血平处理后作用明显增强, 排除了主要是间接作用的可能, 并认为是由于其直接作用的增敏所致。Eph对大鼠血压⁽¹⁰⁾和兔主动脉⁽¹¹⁾的作用亦有相似表现。结果提示, 在豚鼠门静脉, Eph的作用与Phe相似, 主要为直接作用于突触后 α -受体, 而Tyr则主要通过其释放的 NE间接作用于 α -受体。

一定条件的电场刺激能引起神经末梢释放递质, 本文用河豚毒素和酚妥拉明证明电场刺激引起的门静脉收缩是释放的 NE作用于效应器 α -受体所致。Eph和Tyr都能明显增加电场刺激所致门静脉的收缩幅度, 而Phe在低浓度时则不影响(Fig 2)。Phe是一选择性突触后 α -受体激动剂, 一般认为低浓度无突触前作用, Eph和Tyr能增强电场刺激引起的收缩, 可能由于两者均有促进 NE释放的作用。 β -受体阻断剂普萘洛尔能拮抗 Eph的作用, 但不影响 Tyr的作用(Fig 2), 提示 Eph对门静脉的间接作用, 可能与其激活去甲肾上腺素能神经末梢突触前 β -受体, 促进 NE释放有关, 而 Tyr则通过置换神经末梢囊泡 NE从而促进

NE 释放, 与突触前受体关系不大。高浓度 Eph (0.3 mmol/L) 能抑制电场刺激所致收缩 (Fig 2) 的原因, 尚待研究。

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中国药理学报 *Acta Pharmacologica Sinica* 1990 Mar, 11 (2) : 133-137

可乐定和去甲肾上腺素对有或去内皮兔肺动脉条的影响

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Effects of clonidine and norepinephrine on rabbit pulmonary artery strips with or without endothelium¹

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ABSTRACT Relaxing responses of strips of rabbit pulmonary artery (RPA) with endothelium (+E) to norepinephrine (NE) during sustained contraction with KCl 20 mmol/L in the presence of propranolol (Pro) 10 μ mol/L and prazosin (Pra) 1 μ mol/L were more sensitive than those without endothelium (-E) to NE. These responses were inhibited by yohimbine (Yoh) 1 μ mol/L

L. However, the relaxing responses of the strips to clonidine (Clo) were not different between RPA strips +E and -E in the presence of Pro + Pra or Pro + Pra + Yoh 1 μ mol/L.

Relaxing responses of RPA strips -E precontracted by phenylephrine (PE) 1 μ mol/L to Pra and Clo were greater than that of those precontracted by KCl 20 mmol/L. The relaxing responses of these strips precontracted by PE to Pra were larger than those precontracted by Clo 3 μ mol/L; but that of those precontracted by PE and Clo to Yoh were not different.

The results suggest that integrity of the endothelium is an important factor in the relaxing responses of RPA strips to NE. The relaxing effect of Clo on RPA strips precontracted by KCl 20 mmol/L may be due to α_1 -adrenoceptor blockade on smooth muscle cells of the RPA strips.

KEY WORDS vascular endothelium; vascular

Received 1988 Oct 15 Accepted 1989 Jul 3

¹ Project Supported by the National Natural Science Foundation of China, No 86031203