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(3)

心内膜调控离体豚鼠乳头状肌收缩反应

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R 331.36

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摘要 选择性去除心内膜使离体豚鼠乳头状肌 PT 降低(3.2± 0.2 *vs* 4.4± 0.4 mN / mm^2), 其不受刺激频率的影响且± dT/dt_{max} 没有相应改变. 增加外钙浓度该作用减弱. 同时收缩反应时程缩短、舒张反应提前出现($RT_{\frac{1}{2}}$: 77± 10 *vs* 108± 26 ms), 刺激时程– 阈电压曲线轻度左移. 结果表明心内膜对心肌收缩反应具有特征性的调节作用.

关键词 心内膜; 心肌收缩; 乳头状肌; 钙; 电生理学

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Effects of rhynchophylline on motor activity of mice and serotonin and dopamine in rat brain[1]

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ABSTRACT Rhynchophylline (Rhy) reduced the spontaneous motor activity and enhanced the sedative and hypnotic effects of sodium pentobarbital in mice. The effects of Rhy on serotonin (5–HT) and dopamine (DA) concetrations in rat brain, and the release of 5–HT and DA from the regional brain slices were studied by a fluorescence detector. Rhy increased the 5–HT content in the hypothalamus and cortex, but reduced the DA concentrations in the cortex, amygdala, and spinal cord. Rhy promoted the release of endogenous DA from 4 brain regions. The release of 5–HT was increased in 2 brain regions and decreased in hypothalamus slice. However, Rhy inhibited the release of both 5–HT and DA evoked by high potassium.

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KEY WORDS rhynchophylline; motor activity; hypnotics and sedatives; serotonin; dopamine; central nervous system

Uncaria rhynchophylla (Miq) Jackson is a traditional Chinese herb. The total alkaloids of *Uncaria rhynchophylla* has a sedative effect[1]. Rhynchophylline (Rhy), the main alkaloid of *Uncaria rhynchophylla*, has hypotensive and bradycardic effects in anesthetized and concious animals[2,3].

The present study was to investigate its calmative effect and the changes of 5-HT and DA in the central nervous system.

MATERIALS

Rhy crystal was provided by Guangxi Institute of Traditional Chinese Medicine and Materia Madica. It was dissolved in HCl 0.1 mol· L^{-1} and diluted with distilled water to pH 6.5. The serotonin creatinine sulfate and dopamine hydrochloride were purchased from Sigma. Light-sensitive count meter (GJ-1, Tianjin Medical Equipment Factory) and fluorescence spectrometer (RF-540, Shimdzu) were used. The BALB/C mice and Wistar rats of either sex were supplied by the Experimental Animal Center of our college.

METHODS AND RESULTS

Righting reflex Twenty-one mice of either sex, weighing 21.4± *s* 2.9 g, were randomly divided into 3 groups. Group A ip normal saline (NS), group B ip sodium pentobarbital (SP) 35 mg· kg^{-1}, and group C ip SP 35 mg· kg^{-1} plus Rhy 10 mg· kg^{-1}. The righting reflex was normal in group A, while all mice in groups B and C lost the reflex for 13± 6 and 51± 13 min, respectively ($P<0.01$).

Another 28 mice, weighing 22.3± 2.9 g, were randomly divided into 4 groups, injected ip SP 20 mg· kg^{-1}, SP plus Rhy 20 or 40 mg· kg^{-1}, and only Rhy 40 mg· kg^{-1}, respectively. In 2 h, the righting reflex was retained in groups A, B, and D. But in group C 5/7 mice lost their reflex ($P<0.01$).

Spontaneous motor activity Twenty mice, weighing 21.6± 2.4 g, were randomly divided into 2 groups. Mice were put in the box with a light-sensitive count meter 50 min after ip Rhy (20 mg· kg^{-1}) or NS. In the control group, the number of motor activity was 17± 5 times· min^{-1}. Rhy reduced the number to 6± 3 times· min^{-1} ($P<0.01$).

5-HT and DA contents in brain Thirty-four rats, weighing 180± 20 g, were randomly divided into 3 groups. Mice were injected ip NS or Rhy 20 and 40 mg· kg^{-1} at 9 AM, respectively. The rats were decapitated 50 min after medication. The hypothalamus, frontal cortex, brain stem, amygdala, and spinal cord were separated[4]. 5-HT and DA were extracted[5] and measured by RF-540 fluorescence spectrometer.

In this study, the extraction rates of 5-HT and DA were 81.2± 2.1% and 78.9± 2.4%, respectively, similar to those reported previously[5]. The correlation coefficients of 5-HT and DA concentration were 0.9964± 0.0043 and 0.9897± 0.0058, respectively.

The 5-HT content was increased in hypothalamus by Rhy dose-dependently, but decreased in amygdala at a dose of 40 mg· kg^{-1}. Rhy reduced dose-dependently DA the content in the hypothalamus, cortex, and spinal cord (Tab 1).

Release of 5-HT and DA The brain slices of hypothalamuse, cortex, amygdala and brain stem were made[4] from another 45 rats. The slices were immersed in ice-cold artificial cerebrospinal fluid (ACSF)[6] for washing. Then the slices were incubated in ACSF 1.0 ml aerated with 95% O_2+5% CO_2 at 37℃. After 10 min, the ACSF was collected for 5-HT and DA determinations.

In normal potassium (KCl 5 mmol· L^{-1}) ACSF, Rhy (3 and 30 μmol· L^{-1}) reduced the release of 5-HT in the hypothalamus slices ($P<0.01$), and increased the release in the cortex and amygdala at a concentration of 30 μmol· L^{-1} ($P<0.05$). However, Rhy increased the release of DA in all slices (Tab 2).

The releases of both transmitters evoked by high K^+ (KCl 50 mmol· L^{-1}) were more than those in normal K^+ ($P<0.01$). Rhy 30 μmol· L^{-1} lost the effect of 5-HT release induced by high K^+ in hypothalamus and amygdala slices, but enhanced the

Tab 1. Effect of rhynchophylline (Rhy) on serotonin (5-HT) and dopamine (DA) contents in rat brain. $\bar{x}\pm s$. $^{*}P>0.05$, $^{**}P<0.05$, $^{***}P<0.01$ *vs* **Control. Number of specimen in parentheses.**

Transmitter	Brain region	Control	Rhy 20	40 mg · kg^{-1}
5-HT / ng · g^{-1}	Hypothalamus	1 109± 49 (7)	1 383± 63 (11)**	1 378± 76 (11)**
	Cortex	858± 79 (9)	842± 43 (12)*	876± 37 (13)*
	Brain stem	1 009± 49 (8)	1 043± 49 (12)*	1 015± 81 (11)*
	Amygdala	737± 58 (7)	776± 49 (11)*	900± 63 (10)**
	Spinal cord	1 071± 59 (8)	1 027± 57 (12)*	966± 155 (11)*
DA / ng · g^{-1}	Hypothalamus	574± 55 (9)	630± 150 (8)*	730± 130 (8)*
	Cortex	3 633± 402 (9)	2 310± 413 (9)**	1 683± 357 (8)***
	Brain stem	223± 16 (8)	261± 48 (8)*	330± 55 (9)*
	Amygdala	1 586± 209 (8)	823± 119 (8)***	747± 77 (8)***
	Spinal cord	252± 39 (8)	262± 55 (8)*	146± 20 (8)**

Tab 2. Effect of Rhy on release of endogenous 5-HT and DA from rat brain slices. $\bar{x}\pm s$. $^{*}P>0.05$, $^{**}P<0.05$, $^{***}P<0.01$ *vs* **Control.**

	5-HT / ng · g^{-1}			DA / ng · g^{-1}		
	Control	Rhy 3	30 μmol · L^{-1}	Control	Rhy 3	30 μmol · L^{-1}
Hypothalamus	118± 12 (16)	84± 13 (10)***	44± 10 (8)***	87± 8 (26)	97± 12 (9)*	188± 20 (8)***
Cortex	43± 4 (22)	50± 8 (10)*	60± 12 (8)**	43± 5 (22)	51± 6 (7)*	76± 14 (10)**
Brain stem	78± 6 (25)	69± 12 (10)*	64± 5 (9)*	34± 4 (16)	63± 9 (9)***	67± 9 (9)***
Amygdala	96± 9 (21)	82± 12 (8)*	147± 23 (8)**	303± 41 (18)	307± 45 (8)*	355± 77 (8)**

release of 5-HT in brain stem slices ($P<0.05$). But Rhy showed an inhibitive effect on the DA release evoked by high K^{+} in all slices of the 4 brain regions (Tab 3).

DISCUSSION

The determination of monoamine transmitters by fluorescence spectrometer is a commonly used method. In our study, the release of 5-HT and DA were slightly different with that found in previous study[4]. We considered that it was due to a difference in the series of rat, and either sex were used in present study.

Rhy enhanced the sedatives and hypnotic effect of sodium pentobarbital, and reduced the spontaneous motor activity, but the hypnotic effect of itself on mice was not observed. These results suggested that Rhy has a calmative effects, and its effect on the central nervious system was different from pentobarbital.

It is well known that 5-HT and DA are related to

Tab 3. Effect of Rhy on release of endogenous 5-HT and DA by KCl 50 mmol · L^{-1} from rat brain slices. $\bar{x}\pm s$. $^{*}P>0.05$, $^{**}P<0.05$, $^{***}P<0.01$ **KCl** *vs* **Control and KCl+Rhy (30 μmol · L^{-1})** *vs* **KCl.**

	5-HT / ng · g^{-1}			DA / ng · g^{-1}		
	Control	KCl	Rhy+KCl	Control	KCl	Rhy+KCl
Hypothalamus	104± 16 (9)	176± 22 (19)***	98± 19 (7)**	84± 10 (9)	134± 41 (10)**	104± 24 (7)**
Cortex	39± 8 (9)	77± 7 (20)**	67± 10 (7)*	44± 8 (9)	106± 17 (8)**	59± 10 (7)**
Brain stem	74± 9 (9)	92± 8 (15)**	123± 13 (7)**	35± 7 (9)	67± 13 (10)***	21± 5 (7)***
Amygdala	95± 12 (9)	276± 33 (15)***	186± 24 (7)**	303± 49 (9)	727± 140 (15)***	379± 61 (7)**

sleeping, awakening, and emotion[7]. We assumed that the sedatives effect of Rhy resulted from the changes of 5-HT and DA in central nervous system. 5-HT and DA are the monoamine transmitters, but the effects of Rhy on the contents and releases of both them were difference in some brain regions. It seemingly indicated that the effect of Rhy on the transmitters can not be interpreted simply as the reserpine. However, the detailed mechanism of the 5-HT and DA changes, and the relation between the contents and releases of 5-HT and DA remained unclear. Some of the calcium channel blockers reduced the releases of 5-HT and DA by blocking the influx of calcium[8]. Previous studies showed that Rhy may be a calcium blocker[9,10]. It was not difficult to appreciate the effects of Rhy on the releases of 5-HT and DA evoked by high K^+. However, Rhy increased mainly the releases of 5-HT and DA in normal ACSF. We assumed that the effect of Rhy on the releases of the transmitters was performed by another mechanism in the condition, which is to be further explored.

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114-117

(4)

钩藤碱对小鼠活动和大鼠脑内 5-羟色胺及多巴胺的影响

R 965.2

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摘要 钩藤碱(Rhy)使小鼠的自发活动减少, 加强戊巴比妥的镇静催眠作用. 采用荧光分光光度法测定大鼠脑内单胺递质, 显示 Rhy 能增加下丘脑和杏仁核 5-HT 含量, 而皮层、杏仁核和脊髓的 DA 减少. 培养的大鼠脑片中 Rhy 使 DA 释放增加, 5-HT 释放增加见于皮层和杏仁核, 但下丘脑 5-HT 释放减少. 对高 K^+所致的 5-HT 及 DA 释放则表现为抑制作用.

关键词 钩藤碱; 运动活动; 催眠剂和镇静剂; 血清素; 多巴胺; 中枢神经系统