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Cardiovascular effects of intracerebral injection of neuropeptide Y in rats[1]

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ABSTRACT Cardiovascular effects of microinjection of neuropeptide Y (NPY) (25, 50, and 100 pmol / site) into field CA3 of hippocampus (CA3), lateral septal nuclei (LSN) and substantia nigra (SN) were investigated in urethane-anesthetized rats. NPY administered into CA3 produced a dose-dependent hypotension and bradycardia. Maximal changes of mean arterial blood pressure (MAP) were -1.5 ± 0.7, -2.0 ± 0.4, and -4.2 ± 1.6 kPa, respectively; maximal changes of heart rate (HR) were -7 ± 14, -23 ± 24, and -64 ± 50 bpm, respectively. NPY microinjection into LSN produced a dose-dependent increase in MAP (0.9 ± 0.8, 1.3 ± 0.5, and 3.1 ± 0.5 kPa, respectively) and a prominent increase in HR (14 ± 15, 41 ± 28, and 42 ± 31 bpm, respectively), but the tachycardia was not dose-dependent. NPY applied into SN elicited a dose-dependent decrease in MAP (-1.0 ± 0.5, -2.2 ± 0.9, and -4.3 ± 2.0 kPa, respectively), but no statistically significant change in HR. The results showed that exogenously applied NPY has distinct cardiovascular effects in CA3, LSN, and SN.

KEY WORDS neuropeptide Y; blood pressure; heart rate; hippocampus; septal nuclei; substantia nigra

Neuropeptide Y(NPY), a 36 amino acid peptide, is widely distributed over the peripheral and central nervous system[1]. Recent evidence indicated that NPY was putatively involved in cardiovascular control and has been located immunohistochemically in important cardiovascular centers in brain[2,3]. Studies based on a receptor binding technique using membrane fractions showed that the receptors of NPY exist in the filed CA3 of hippocampus (CA3), lateral septal nuclei (LSN) and substantia nigra (SN) of rats[4]. The purpose of the present study was to determine the effects of NPY administered into CA3, LSN and SN on cardiovascular system in anesthetized rats.

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MATERIALS AND METHODS

Wistar rats of either sex weighing $229 \pm s$ 16 g were used. Rats were anesthetized with urethane (1.2 g · kg^{-1}, ip). The femoral artery was cannulated with polyethylene tubing for recording arterial blood pressure and heart rate. The animals were then placed in a stereotaxic instrument. A small craniotomy was performed and NPY or vehicle was injected into CA3, LSN, and SN in a volume of 0.3 μl during 1 min with 1 μl microsyringe. Rectal temperature was monitored and maintained in the range 37.5-38.5℃ with a heating blanket. At the end of the experiments, the brain was fixed in 10% formalin and 40 μm sections cut for histological identification of the injection sites.

NPY (Sigma) was dissolved in 0.9% saline (pH 7.0).

RESULTS

Cardiovascular effects of NPY in CA3 Microinjection of NPY (25, 50, 100 pmol / site) produced a dose-dependent hypotension and bradycardia. The cardiovascular effects began between 1 and 5 min and maintained between 10 and 130 min after administration of the peptide. The hypotensive effects elicited by microinjection of 25, 50, and 100 pmol NPY into CA3 peaked at 7 ± 7, 22 ± 10, and 49 ± 29 min postinjection, respectively; the bradycardic effects, at 6 ± 4, $19 \pm$

13, and 35 ± 7 min postinjection, respectively. Saline microinjection into CA3 or NPY microinjection into peripheral regions of CA3 did not show hemodynamic responses (Tab 1).

Cardiovascular effects of NPY in LSN NPY microinjection into LSN resulted in a significant increase in mean arterial blood pressure (MAP) and heart rate (HR). The pressor responses were dose-dependent while the tachycardic effects, not. The appearance of the effects varied from 2–10 min; the recovery, from 10–120 min after administration of 25, 50, and 100 pmol into LSN. The peak effects of NPY (25, 50, and 100 pmol / site) in MAP were reached at 12 ± 9, 24 ± 7, and 33 ± 20 min, respectively; in HR, at 22 ± 8, 35 ± 14, and 25 ± 15 min, respectively. No prominent cardiovascular response could be recorded after NPY injection into peripheral regions of LSN or saline injection into LSN (Tab 1).

Tab 1. Maximal changes of mean arterial blood pressure and heart rate after NPY microinjection into CA3, LSN, and SN. $n = 6–7$, $\bar{x} \pm s$, $^{*}P > 0.05$, $^{**}P < 0.05$, $^{***}P < 0.01$ *vs* **control.**

	CA3	LSN	SN
Maximal change of mean arterial blood pressure / kPa			
Control	0.1 ± 1.0	−0.4 ± 0.7	−0.2 ± 0.7
NPY			
25 pmol	−1.5 ± 0.7**	0.9 ± 0.8**	−1.0 ± 0.5**
50 pmol	−2.0 ± 0.4***	1.3 ± 0.5***	−2.2 ± 0.9***
100 pmol	−4.2 ± 1.6***	3.1 ± 0.5***	−4.3 ± 2.0***
Maximal change of heart rate / bpm			
Control	−10 ± 15	−3 ± 14	−2 ± 31
NPY			
25 pmol	−7 ± 14*	14 ± 15*	−5 ± 6*
50 pmol	−23 ± 24*	41 ± 28***	−5 ± 24*
100 pmol	−64 ± 50**	42 ± 31***	−26 ± 24*

Cardiovascular effects of NPY in SN A dose-dependent decrease in MAP was elicited by microinjection of NPY (25, 50, and 100 pmol / site), but no significant change in HR statistically. The depressor effects appeared between 1 and 4 min following NPY administration into SN. The duration of the hypotension is 20–120 min. The time of the peak effects in MAP was respectively 12 ± 8, 25 ± 13, and 33 ± 15 min. Administration of saline in SN and NPY in peripheral regions of SN did not give rise to any significant cardiovascular changes (Tab 1).

DISCUSSION

CA3, LSN and SN, the structures associated with the central control of cardiovascular activities[5–9], contained the higher concentrations of NPY receptors[4]. Although the central cardiovascular effects of NPY remain at present putative[2], the cardiovascular effects elicited by NPY administration in CA3, LSN, and SN are unclear. In the present study, NPY microinjection into CA3 caused a dose-dependent hypotension and bradycardia, but saline microinjection into CA3 or NPY microinjection into peripheral regions of CA3 did not produce hemodynamic responses, indicating that the cardiovascular effects produced by NPY microinjection into CA3 exhibit regional specificity. NPY administration in LSN results in significant increase in MAP and HR in which the pressor reaction is dose-dependent. No significant change in MAP and HR could be recorded after NPY injection into peripheral regions of LSN or saline injection into LSN. These results suggested that exogenous NPY in LSN could produce a specific cardiovascular effect. NPY microinjection into SN elicited a dose-dependent decrease in MAP, but administration of saline in SN and NPY in peripheral regions of SN do not give rise to any significant cardiovascular changes, which demonstrates NPY applied into SN could produce a specific depressor effect. It is note-worthy that the diverse cardiovascular responses to microinjection of NPY into CA3, LSN, and SN

have been ascertained.

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大鼠脑内注射神经肽 Y 的心血管效应

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提要 麻醉大鼠海马 CA3 区(CA3)内微量注射神经肽 Y(NPY)引起剂量依赖性血压下降和心率减慢. 外侧隔核(LSN)内微量注射 NPY 引起血压升高和心率加快，其中血压升高是剂量依赖性的，但心率加快则没有剂量依赖性. 黑质(SN)内微量注射 NPY 引起剂量依赖性血压下降，但心率在统计学上无明显变化. 结果表明，外源性 NPY 在 CA3，LSN 和 SN 有明显的心血管效应.

关键词 神经肽 Y; 血压; 心率; 海马; 隔核; 黑质

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Rate– and voltage–dependent effects of *m*–nisoldipine on action potential of partially depolarized guinea pig papillary muscle

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ABSTRACT The rate– and voltage–dependent effects of *m*–Nis were studied using standard microelectrode technique and real–time microcomputer analyzing system. The onset rate for rate–dependent inhibition (RDI) on action potentials of partially depolarized papillary muscle of guinea pig was accelerated as the concentration of *m*–Nis was increased from 0.5 to 2 $\mu mol \cdot L^{-1}$ or the driving frequency decreased from 0.8 to 0.2 Hz. The steady–state values of V_{max} and APA were markedly decreased by elevating the concentration of *m*–Nis or increasing the driving frequency. The recovery time constants of V_{max}, APA, and latency period from RDI were all increased by *m*–Nis (1 $\mu mol \cdot L^{-1}$). The inhibitory

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