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Effects of argipressin injected into medial amygdaloid body on blood pressure and heart rate in rats

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ABSTRACT Graded injections of argipressin (Arg, 150, 300, and 600 ng / 1.5 μl CSF, 2 min) into the medial amygdaloid body in anesthetized rats produced a dose-related increase in the mean arterial pressure and heart rate (Maximal ΔMAP = 2.9± 1.5 kPa, Maximal ΔHR = 67± 38 bpm), which lasting > 40 min at 600 ng dosage. Naloxone (15 μg / 15 μl CSF) injected into the lateral ventricle blocked the cardiovascular responses to Arg. These results suggest that Arg exerts a central action on the cardiovascular system via the opioid in the lateral ventricle.

KEY WORDS argipressin; naloxone; amygdaloid body; blood pressure; heart rate

Medial amygaloid body is implicated in blood pressure regulation[1,2]. Our laboratory has demonstrated that paraventricular nucleus excited the medial amygdloid body through the release of Arg[3]. The present study was designed to assess the role of Arg in medial amygdaloid body as a putative regulator of blood pressure (BP) and heart rate (HR).

MATERIALS AND METHODS

Wistar rats of either sex (n = 47, weighting 307 ± s 27 g) were anesthetized with ip urethane 1 g · kg^{-1}. Two single-barre metallic micropipettes were stereotaxically implanted into the medial amygdaloid body and later ventricle separately.

Both argipressin (Arg, Sigma) and the endorphin receptor blockader naloxone (Nal, Endo Laboratories) were dissolved in artificial cerebrospinal fluid (CSF) (Arg 150, 300, and 600 ng / 1.5 μl CSF; Nal 15 μg / 15 μl CSF). Pure CSF (both 1.5 μl and 15 μl) were used as control groups to avoid the effects of no-specific stimulation, such as volume, pH, temperature, velocity of injection and others.

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The carotid artery was cannulated with a plastic cannula filled with 1% heparin. The cannula was connected with a pressure transducer (BPM-II) coupled to a recorder.

After completion of the experiments all rats were decapitated. Brains were fixed in 10% formalin. Serial frozen sections (50 μm) were carried out in a cryostat for histological verification of injector tip placement.

All values presented were $\bar{x}$± s. Group comparison t test was used.

RESULTS

Effect of Arg injected into medial amygdaloid body Arg 150 ng produced a rapid and prominent rise of BP in all 8 rats with a maximal response at 5 min after injection (ΔMAP = 1.2± 0.7 kPa) and a slight rise of HR (ΔHR = 9± 4 bpm). Arg 300 ng produced a greater effects. Arg 600 ng produced most marked hypertensive effect with a maximal respone appearing at 15 min after injection (ΔMAP = 2.9± 1.5 kPa) and strongest tachcardiac effect (ΔHR = 67± 38 bpm).

Nal pretreatment on Arg effects The rats were treated 10 min before injection of Arg with icv of Nal 15 μg / 15 μl CSF in 2 min, the cardiovascular effects of Arg in medial amygaloid body were attenuated.

Tab 1. MAP and HR responsed to 600 ng Arg injected into the medial amygaloid body in intact and post icv naloxone (Nal). n = 8 rats, $\bar{x}$ ± s. $^{**}P < 0.05$, $^{***}P < 0.01$ *vs* Arg 600 ng group without Nal. $^{*}P > 0.05$ *vs* before.

Arg / ng	Nal / μg	MAP / kPa	HR / bpm
600	0	13.6± 1.1	420± 60
600	15	11.5± 1.2**	400± 60***
0	15	9.3± 0.6*	400± 40*

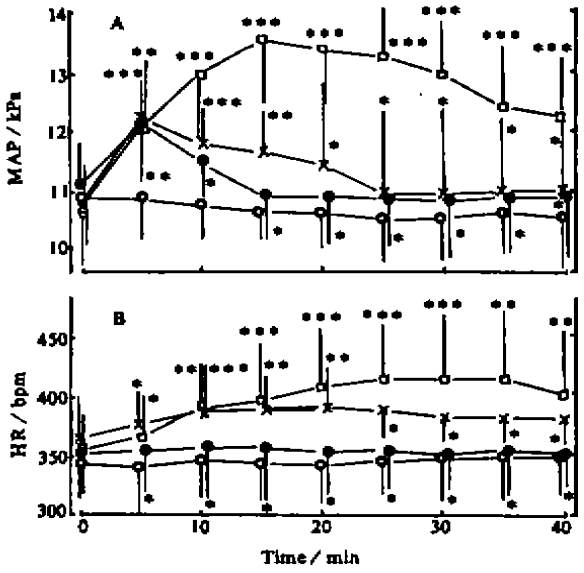

Fig 1. Mean arterial pressure (MAP) (A) and heart rate (HR) (B) after microinjection of argipressin (Arg) into the medial amygaloid body. Artificial cerebrospinal fluid (○), Arg 150 (●), 300 (×), and 600 ng (□). *n*= 8 rats. $\bar{x} \pm s$. * $P > 0.05$, ** $P < 0.05$, *** $P < 0.01$ *vs* before.

DISCUSSION

The main finding of the present study was that injection of Arg into the medial amygdaloid body produced a dose-responed increase of mean arterial pressure and heart rate. This finding is consistent with the hypothesis that Arg plays a central role in cardiovascular regulation[4-6]. This excitatory effect of Arg appears to be specific for this peptide comparing with the fact that injection of CSF into the medial amygdaloid body had little effect on arterial pressure and heart rate. The present results first demonstrated that Arg-containing fibers in the medial amygdaloid body of the forebrain participated in cardiovascular regulation[7-10]. This result suggests that the medial amygdaloid body is sensitive to Arg in regulating autonomic functions. The fact that intra-medial amygdaloid body administration of Arg produced cardiovascular effects is consistent with the reports that the lesion of the amygdala block or attenuate learned cardiovascular responses to stress- or fear-inducing stimuli[11-13] and is in accordance with the distribution of argipressinergic pathways[14,15]. Comparing that of the neuronucleus in brain stem, the regulating function of amygdaloid body on cardiovascular action is relatively complex. In brain stem, the electrical stimulation of locus coeruleus or dorsal vagal nuclei produces coeruleus or dorsal motor vagus produces separately simple hypertension or hypotension. However, the electrical stimulation of amygdaloid body produces complex change of blood preasure including hypertension and hypotension. In present study, we observed that the time of appearing maximal blood preasure change in 600 ng Arg group was later than that in 300 ng Arg group. The result may relate to aforementioned reason.

The mechanisms by which injection of Arg into the medial amygdaloid body produces cardiovascular alterations remain speculative. Increase in the mean arterial pressure and heart rate in response to injection of Arg into the medial amygdaloid body was attenuated by pretreatment of icv of endorphin receptor blockader Nal. These results suggested that injection of Arg into the medial amygdaloid body induces an increase in heart rate and blood pressure due to, in part, a release of opioid in the lateral ventricles. However, we can not rule out the possibility that Nal blocked directly the Arg receptor in medial amygdaloid body.

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118–120 (5)

杏仁核内微量注射精氨酸加压素对大鼠血压和心率的影响

R965.2

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摘要 向麻醉大鼠杏仁核内注射精氨酸加压素 150, 300 和 600 ng (溶于 1.5 μl 人工脑脊液, 2 min 内注完) 可产生剂量依赖性血压升高, 心率加快, 在 600 ng 加压素剂量, 血压升高 2.9± 1.5 kPa, 心率加快 67± 38 bpm. 作用时间超过 40 min. 预先在侧脑室注入阿片受体阻断剂纳络酮 15 μg (溶于 15 μl 人工脑脊液, 2 min 内注完)可部分阻断上述升压, 加快心率效应.

关键词 精氨酸加压素; 纳络酮; 杏仁核; 血压; 心率