兽类学报1997, 17 (3): 204～207
Acta Theriologica Sinica

NOREPINEPHRINE STIMULATES THE RELEASE OF CORTICOTROPIN-REALEASING FACTOR FROM MEDIAN EMINENCE OF *OCHOTONA CURZONIAE* *

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Abstract

We studied the effect of neurotransmitter norepinephrine (NE) on immunoreactive corticotropin-releasing factor (CRF) of median eminence (ME) in the native pika (*Ochotona curzoniae*). At one hour after intracerebroventricular (icv) administration of NE in doses of 3.75, 7.5, 15 and 30 μg/100 g BW, the CRF level of ME increased. And the plasma corticosterone concentration also increased. Two and six days after adrenalectomy (ADX), NE concentration in hypothalamus declined to 76.32% and 76.27% of those in intact pika, plasma corticosterone concentration also decreased to 16.57 and 2.05% of the control. These results indicated that NE have a effect on activating HPA axis through activating hypothalamic CRF in *Ochotona curzoniae*.

Key words *Ochotona curzoniae*; Corticotropin-releasing factor; Norepinephrine

CRF is a major component in the activation of the hypothalamo-pituitary-adrenal (HPA) axis under stress condition (Rivier et al., 1986). A large number of evidence indicates that central catecholamines play an important role in the regulation of ACTH secretion, presumably through stimulation of the release of CRF and vasopressine (Guillaume et al., 1987). Electron microscopic studies have shown that there is direct synapses between CRF containing neurons and terminals that contain tyrosine hydoxylase and phenylethanolamine-N-methyltransferase (Liposits et al., 1986; Liposits et al., 1986). Selective lesions of ventral noradrenergic ascending bundle induce a marked reduce of CRF from ME (Alonso et al., 1986). These studies indicate catecholamines are involved in CRF releasing in rats hypothalamus. Pika is a native plateau small mammals, in which the role NE plays in releasing of CRF in hypothalamus is unclear. The aim of present study is to determine the effect of NE on CRF secretion from ME in pika and the concentration changes of NE in hypothalamus and plasma corticosterone after ADX.

MATERIALS AND METHODS

* The abstract of the paper was published in proceeding of XVIII Chinese physiological conference. Nov. 1989, Shanghai.
Received 12 July 1996, Accepted 6 December 1996

The pika were captured from Haibei area, Alpine Meadow Ecosystem Research Station, Academia Sinica, Qinghai province, then kept in feeding facility in Xining for one month (light on from 8: 00～20: 00), before the experiments. The pika weighed 140±20 g. All experiments were designed as Randomized Experiments. Bilateral adrenalectomized pika were only supplied with 0.9% saline water. Icv injections NE were performed under slightly anesthesia with sodium pentobarbital (40 mg/kg BW, ip), introducing 2 μl into each third ventricle. Blood samples and ME were collected by decapitation one hour after icv administration of NE.

Hormone measurement: CRF levels were assayed by specific radioimmunoassays (RIA) as described previously (Du et al., 1992). Plasma corticorsterone and NE concentration were estimated by flurometric method (Zenker et al., 1958).

All data were presented as mean (SD and the differences among samples were tested by student T-test.

RESULT

1. Effect of NE on CRF release

Fig. 1 showed the effects of icv injection of NE on CRF levels in ME. All NE treated-animals showed the increase of CRF levels in ME compared with untreated group. One hour after administration different doses of NE 3.75, 7.5, 15 and 30 μg/100 g BW, CRF levels in ME rose to 106.05% (10.16±2.81 ng/mg protein), 135.28% (12.96±2.43 ng/mg protein, $P < 0.05$), 138.94% (13.31±1.83 ng/mg protein, $P < 0.01$) and 103.65% (9.93±1.09 ng/mg protein) of control group (9.58±1.62 ng/mg protein). Icv NE also induced a corticosterone concentration increase (Fig. 2).

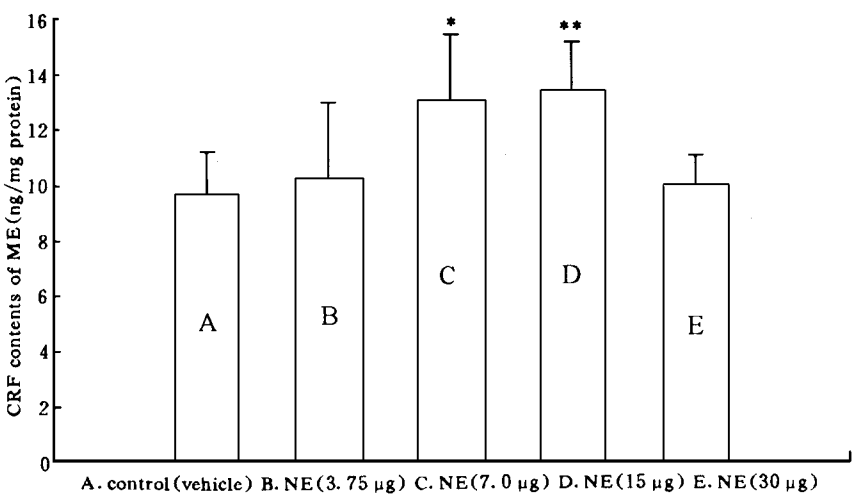

Fig. 1 Effects of NE icv on CRF content of ME in *Ochotona curzoniae*

N = 6; * $P < 0.05$; * * $P < 0.01$ *vs* control

2. Influence of ADX on hypothalamic NE, CRF levels in ME and plasma corticosterone

Two and six days after ADX, the content of NE in hypothalamus significantly re-

duced to 76.32% ($P < 0.01$) and 76.27% ($P < 0.05$) of control (2.01±0.31 μg/g fresh tissue). Plasma corticosterone concentration also reduced to 16.57% ($P < 0.01$) and 2.05% ($P < 0.001$) of Sham operated animals (8.27±4.11 μg/100 ml, Table 1).

Table 1 **Influences of ADX on NE concentration in hypothalamus and plasma corticorsterone concentration (CORT)**

	SHAM	ADX (2d)	ADX (6d)
NE	2.01±0.31 (6)	1.53±0.18 (7)**	1.53±0.33 (6)*
CORT	8.27±4.11 (7)	1.37±2.06 (7)**	0.17±0.27 (6)***

The values represent Mean±SD, Numbers showed in parentheses are the numbers of subjects;
* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$

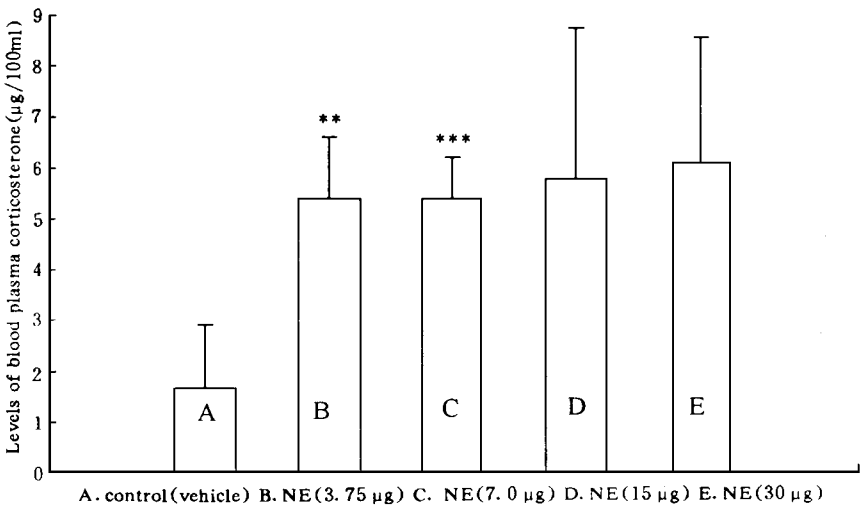

Fig. 2 Effects of NE icv on levels of blood plasma corticosterone of *Ochotona curzoniae*
N = 5; * $P < 0.05$; *** $P < 0.001$ *vs* control

DISCUSSION

The present experiments demonstrated the stimulatory action of NE at hypothalamic level to evoke secretion of CRF and thus to activate the pituitary-adrenal cortex axis in pika. Plotsky (1987) also found similar evidence suggesting a facilititory action of central catecholamines on the hypothalamo-pituitary-adrenal cortex axis, but was contrary to the models of NE playing a inhibitory action to CRF release from cultured hypothalamus of rats in vitro (Jones et al., 1976). When administrating NE of 30 μg/100 g BW, CRF secretion remained unchanged in our experiment, presumably, which was be resulted from that different types or subtypes of NE receptor were involved at different concentration of NE. However, what type of receptors was involved in regulation of secretion of CRF by central NE in pika are did not know. The concentrations of hypothalamic NE, and plasma corticosterone in ADX pika all reduced compared with intact animals. We have demonstrated that CRF levels in ME of pika noticeable declined ($P < 0.05$) compared with control at 2 d after ADX (Du et al., 1992). These evidence suggest-

ed that corticosterone may play an important role in maintaining central NE level and CRF neuron activity in hypothalamus.

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中 文 摘 要

去甲肾上腺素刺激高原鼠兔CRF的分泌

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用脑室注射神经递质去甲肾上腺素(NE)和RIA法测定下丘脑正中隆起处促肾上腺皮质激素释放激素(CRF)水平，研究NE对高原鼠兔下丘脑CRF分泌的作用。脑室给予不同剂量NE 3.75，7.5，15，30 μg/100 g BW. 正中隆起(ME)处CRF含量分别增加到对照组的106.05%，135.28% ($P < 0.05$)，138.94% ($P < 0.01$)，103.65%，同时，血浆皮质酮浓度也分别增加到对照组的323.35% ($P < 0.01$)，323.35% ($P < 0.001$)，346.71%，366.47%。肾上腺切除后2天和6天时，下丘脑NE下降到对照的76.32% ($P < 0.05$)，76.27% ($P < 0.01$)，血浆皮质酮也下降到16.57% ($P < 0.01$)，2.05% ($P < 0.001$)。上述结果表明，NE刺激高原鼠兔下丘脑CRF的分泌并激活下丘脑垂体肾上腺皮质轴。肾上腺皮质激素对维持下丘脑NE水平和CRF神经元活动有一定的紧张作用。

关键词　高原鼠兔；促肾上腺皮质激素释放激素；去甲肾上腺素