



Original article

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THE ROLE OF AREA POSTREMA IN THE CENTRAL REGULATION OF ARTERIAL BLOOD PRESSURE

SUMMARY

Nicotine, pilocarpine and McN-A-343 (selective agonist of muscarinic M1 receptors) intracerebroventricularly injected to cats caused a dose-dependent decrease in arterial blood pressure. In area postrema lesioned cats, the hypotensive effect of the intracerebroventricularly injected nicotine, pilocarpine and McN-A-343 was significantly attenuated. These authors have found that the results obtained in the experiments suggest that muscarinic M1 and nicotinic receptors of the area postrema mediate in the central regulation of arterial blood pressure.

Key words: area postrema, hypotensive effect, nicotine, pilocarpine

INTRODUCTION

The area postrema is a triangular field of the rhomboid fossa, between the funiculus separans and the gracile tubercle (figure 1). It contains markedly vascularized tissue rich in glia and covered by ependyma. The blood-brain barrier is modified in these regions (1). The area postrema contains numerous neurotransmitter receptors (alpha-adrenergic, nicotinic, muscarinic, opioid and angiotensin II receptors) (2). Numerous studies have shown that the area postrema participates in the regulation of cardiovascular function. The findings of these studies, however, are often contradictory. By stimulating the area postrema, Gatt et al. (1985) showed a decrease in blood pressure and heart rate, whereas Ferguson and Marcus (1988) registered an increase in arterial blood pressure (3,4). Area postrema lesion triggers a long-term elevation in normotensive and spontaneously hypertensive rats (5). In addition, it has been demonstrated that the hypertensive effect

is attenuated if induced by intracerebroventricular injection of angiotensin II to area postrema lesioned animals (6) or by intracerebroventricular NaCl to dogs (7).

MATERIAL AND METHODS

Both male and female cats of 2.0-3.5 kg body weight were used. The cats were anesthetized with pentobarbital-sodium (35-40 mg/kg) injected into the left lateral cerebral ventricle through the Collison cannula according to the method described by Veljkovic et al. 1989 (6).

In order to approach the area postrema, the atlanto-occipital membrane was interrupted. Upon reaching the site, the area postrema was destroyed by electro-coagulation using 5 mA electrical current for 60 seconds.

Arterial blood pressure was measured directly on a kymograph using a mercury manometer that

tion in arterial blood pressure within the range of 18-80 mmHg (figure 2C). The hypotensive effect of nicotine was developed 3-4 minutes following injection, whereupon it attenuated and blood pressure restored to the initial values within 15-20 minutes.

In area postrema lesioned animals the initial values of blood pressure and heart rate prior to nicotine injection were 132.2 ± 6.5 and 168 ± 8.1 /min.

Intracerebroventricular nicotine administered at the same doses caused a markedly attenuated hypotensive effect.

DISCUSSION

Our experiments have demonstrated that intracerebroventricular administration of McN-A-343 (a selective agonist of muscarinic M1 receptors) reduces arterial blood pressure in a dose-dependent manner. Given intracerebroventricularly, pilocarpine (an agonist of muscarinic M1 receptors) and nicotine also caused a dose-dependent hypotensive effect.

In area postrema lesioned animals, intracerebroventricular injection of pilocarpine, McN-A-343 and nicotine led to a significantly decreased hypotensive effect.

On the other hand, area postrema intact and area postrema lesioned animals did not show a significant difference with respect to the acetylcholine-induced hypotensive effect.

Ferguson and Smith (1991) demonstrated that electric stimulation of specific sites of the area postrema is followed by hypotension (4). The above-mentioned hypotensive effect induced by electric stimulation of the area postrema can be eliminated by atropine, a non-selective muscarinic antagonist, and by hexamethonium, a blocker of nicotinic

receptors. Nicotinic and M1 muscarinic receptor sites responsible for cardiovascular response have been identified in the caudal region of the area postrema (8). These findings are consistent with our earlier experiments, demonstrating that the hypotensive effect caused by intracerebroventricular nicotine and McN-A-343 develops with the mediation of nicotinic and muscarinic M1 receptors (9).

In contrast, area postrema lesioned animals did not show any change in the acetylcholine hypotensive effect.

Acetylcholine (as well as other choline esters) develops its central cardiovascular and behavioral effects through the mediation of muscarinic M2 and, possibly, M3 receptors (10,11,12).

Muscarinic M2 receptors have been identified in the nucleus tractus solitarius, a neuronal structure adjacent to the area postrema, thereby allowing various interconnections between the two.

Given that the activation of muscarinic receptors of choline esters leads to hypotension (13) and area postrema ablation does not reduce the hypotensive effect of acetylcholine, the conclusion may be drawn that the hypotension induced by intracerebroventricular injection of McN-A-343, pilocarpine and nicotine does not involve muscarinic M2 receptors. Such assumptions were confirmed by Beleslin and Samardzic 1979, Beleslin and Krstic 1987, Beleslin and Nedelkovski 1989 (14,15,16).

These authors found that intracerebroventricular administration of McN-A-343 and nicotine, but not of choline esters, cause vomiting that may be reduced or prevented by way of ablation of the area postrema.

In conclusion, the results obtained in the experiments suggest that muscarinic M1 and nicotinic receptors of the area postrema mediate in the central regulation of arterial blood pressure.

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ULOGA AREJE POSTREME U CENTRALNOJ REGULACIJI ARTERIJSKOG KRVNOG PRITISKA

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SA@ETAK

Nikotin, pilokarpin i McN-A-343 (selektivni antagonist M1 receptora) ubrizgani intracerebroventrikularno ma-kama su izazvali dozno zavisni pad krvnog pritiska. U ma-aka kod kojih je areja postrema bila razorena, efekat intracerebroventrikularnog ubrizgavanja nikotina, pilokarpina i McN-A-343 bio je zna-ajno manji. Na osnovu dobijenih rezultata autori zaklju-uju da su nikotinski i muskarinski M1 receptori areje postreme uklju-eni u centralnu regulaciju arterijskog krvnog pritiska.

Klju-ne re-i: areja postrema, hipotenzivno dejstvo, nikotin, pilokarpin