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CENTRAL ADRENOCEPTORS AND CHOLINOCEPTORS IN CARDIOVASCULAR CONTROL

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1 In cats anaesthetized with chloralose, adrenoceptor and cholinoceptor agonists and antagonists were localized to the posterior hypothalamus (PH), lateral medullary pressor area (LMPA) and spinal autonomic loci to delineate the role of central cholinoceptors and adrenoceptors in cardiovascular control.

2 All along the neuroaxis, the α-adrenoceptors seem to subserve an inhibitory and the β-adrenoceptors a facilitatory role in cardiovascular control. There appears to be a predominance of α-adrenoceptors at the medullary level and β-adrenoceptors at the hypothalamic level.

3 The nicotinic cholinoceptors at the hypothalamic, medullary and spinal levels were facilitatory, whereas muscarinic cholinoceptors were inhibitory for cardiovascular control. However, muscarinic receptors were undetectable at the posterior hypothalamus.

4 The central cardiovascular effects of nicotine are attributed to nicotinic receptor activation and release of central catecholamines.

5 There appears to be a relationship between central cholinergic and adrenergic mechanisms in cardiovascular control.

Introduction

There is ample evidence to implicate brain catecholamines and acetylcholine in the central control of cardiovascular function. However, pharmacological studies to define their actions, have yielded conflicting results. Intracerebroventricular (i.c.v.) injections of noradrenaline or adrenaline evoked hypotension and bradycardia in cats and dogs (Nashold, Mannarino & Wunderlich, 1962; Bhargava, Misra & Tangri, 1972). On the other hand, both excitatory and inhibitory cardiovascular responses, blocked by propranolol and phentolamine respectively, were reported with i.c.v. adrenaline (Day & Roach, 1974) and isoprenaline (Gagnon & Melville, 1967; Schmitt & Fenard, 1971; Bhargava *et al.*, 1972; Day & Roach, 1974). Moreover, centrally administered clonidine, an α-adrenoceptor agonist, decreased blood pressure, heart rate and sympathetic discharges (Schmitt, Schmitt, Boissier & Giudicelli, 1968).

The central administration of acetylcholine and other cholinomimetic agents in dogs, induced a pressor response and a tachycardia which could be blocked by atropine (Sinha, Dhawan, Chandra & Gupta, 1967; Srimal, Jaju, Sinha, Dixit & Bhargava, 1969; Lang & Rush, 1973). However, variable cardiovascular effects were reported following central administration of cholinomimetic agents in cats (Bhawe, 1958; Armitage & Hall, 1967; Guertzenstein, 1973) and in rats (Brezenoff & Jenden, 1970; Brezenoff, 1972).

The differing results obtained by these investigators may arise from either differences in receptor function at various neuronal sites in the central nervous system (CNS) or the species of animals used. Hence, in the present study an attempt has been made to delineate the cardiovascular function of adrenoceptors and cholinoceptors located in the posterior hypothalamus, lateral medullary reticular pressor area and spinal autonomic loci of the cat.

Methods

Cats of either sex (1.5 kg–4.5 kg) were used. The animals were anaesthetized with α-chloralose (80 mg/kg i.p.), bilaterally vagotomized and maintained on positive pressure artificial respiration. The femoral vein was cannulated with a polythene tube for intravenous injections. Blood pressure was recorded from the femoral or carotid artery with a pressure transducer (P_{23}) and either a Grass Model P5 or Encardiorite

(India) polygraph. The heart rate was determined from the electrocardiogram (Lead II) recorded on another channel of the polygraph.

The drugs were localized in the areas of the CNS by the techniques of superfusion, regional perfusion and intrathecal injections.

The drugs, dissolved in artificial cerebrospinal fluid (CSF, pH 7.2, 37°C; Merlis, 1940), were superfused into the posterior hypothalamus (PH) and lateral medullary reticular pressor areas (LMPA) by means of a push-pull cannula, according to the technique of Philippu, Przuntek & Roensberg (1973), at a rate of 0.1 ml/min for 15 minutes. The placement of the cannula in the PH and LMPA was carried out stereotaxically by means of the coordinates of Snider & Niemer (1961).

We employed regional perfusions from the lateral ventricle to the aqueduct (Bhattacharya & Feldberg,

Table 1 Cardiovascular effects of agents which act on adrenoceptors and cholinoceptors superfused for 15 min into the posterior hypothalamus of cat

Drug (concentration per ml)	*Drug pretreatment (concentration per ml)*	*No. of expts*	*Change in blood pressure (mmHg ± s.e.)*	*Change in heart rate (beats/min ± s.e.)*
Adrenaline (100 μg)	None	6	+13.0 ± 4.2	+10.0 ± 4.0
	Piperoxan (500 μg)	4	+15.0 ± 2.5	+12.0 ± 2.8
	Sotalol (2.0 mg)	4	−1.2 ± 2.4	−3.3 ± 4.4
Isoprenaline (100 μg)	None	3	+20.0 ± 3.6	+15.0 ± 3.1
	Piperoxan (500 μg)	3	+19.3 ± 2.9	+14.0 ± 2.8
	Sotalol (2.0 mg)	3	+1.2 ± 3.3	+3.3 ± 2.9
Clonidine (60 μg)	None	3	−10.0 ± 2.8	−10.0 ± 1.6
	Piperoxan (500 μg)	3	−1.7 ± 1.6	0.0
Acetylcholine (500 μg)	Physostigmine (1.0 mg)	2	+35.0	+35.0
	Ethylbenztropine (2.0 mg)	2	+25.0	+25.0
	Chlorisondamine (2.0 mg)	2	0.0	0.0
	Sotalol (2.0 mg)	2	−2.5	0.0
Carbachol (500 μg)	None	3	+33.3 ± 4.5	+16.6 ± 3.4
	Piperoxan (1.0 mg)	1	+40.0	+10.0
	Chlorisondamine (2.0 mg)	2	−5.0	−5.0
	Sotalol (2.0 mg)	1	0.0	0.0
Nicotine (250 μg)	None	3	+33.3 ± 2.4	+40.0 ± 5.8
	Piperoxan (1.0 mg)	1	+40.0	+40.0
	Chlorisondamine (2.0 mg)	2	+2.5	+5.0
	Sotalol (2.0 mg)	1	+5.0	0.0
Oxotremorine (200–500 μg)	None	2	0.0	0.0
Pilocarpine (5.0–10.0 mg)	None	2	−2.5	0.0

1958), and from IVth ventricle to the cisterna magna, in order to localize the drugs in hypothalamic and medullary areas respectively, and used artificial CSF at a flow rate of 0.1 ml/min for 15 minutes.

Spinal compression vasomotor responses (SCVR) were obtained by compression of the spinal cord (ligated within the meninges at C7) according to the technique of Bhargava & Kulshrestha (1959; 1960) and Bhargava & Srivastava (1970).

Drugs

The drugs used were adrenaline acid tartrate, noradrenaline hydrochloride, clonidine hydrochloride, isoprenaline sulphate, piperoxan hydrochloride, propranolol hydrochloride, sotalol hydrochloride, acetylcholine hydrochloride, carbamylcholine chloride (carbachol), oxotremorine sesquifumarate, pilocarpine nitrate, nicotine hydrogen tartrate, dimethyl phenyl piperazinium (DMPP), physostigmine salicylate, atropine methyl nitrate, ethylbenztropine bromide, chlorisondamine salicylate and 6-hydroxydopamine. All the doses of drugs used in the present study refer to their salts.

Results

Effect of autonomic agents on the cardiovascular loci in the posterior hypothalamus (PH)

The results of this study are summarized in Tables 1 and 2.

Adrenoceptor stimulants. Superfusion of adrenaline (100 μg/ml) or isoprenaline (100 μg/ml) in the posterior hypothalamus elicited a rise in blood pressure (13.0 ± 4.2 and 20.0 ± 3.6 mmHg respectively, mean ± s.e. mean), and heart rate (10.0 ± 4.0 and 15.0 ± 3.1 beats/min, respectively). Prior superfusion of piperoxan (500 μg/ml) in the PH failed to alter significantly these effects of adrenaline and isoprenaline, while superfusion with sotalol (2.0 mg/ml) or propranolol (1.0 mg/ml) completely blocked these responses. Superfusion of clonidine (60 μg/ml) in the PH resulted in a fall of blood pressure and bradycardia which was completely prevented by prior piperoxan treatment.

Similar results were obtained with regional perfusion of the ventricular system from the lateral ventricle to the aqueduct with adrenaline, isoprenaline and clonidine (Table 2).

Cholinoceptor stimulants. Superfusion of acetylcholine (500 μg/ml) in atropine methyl nitrate (1.0 mg/kg i.v.) and physostigmine (1.0 mg/ml superfusion) pretreated cats evoked a pressor response (35.0 mmHg) associated with a tachycardia (35.0 beats/minute). Pretreatment by superfusion with ethylbenztropine (2.0 mg/ml) did not affect the cardiovascular response to acetylcholine while chlorisondamine (2.0 mg/ml) superfusion blocked it. Furthermore, blockade of central β-adrenoceptors by sotalol (2.0 mg/ml) superfusion in the PH also blocked the effects of acetylcholine.

Nicotine (250 μg/ml) or carbachol (500 μg/ml) superfusion into PH induced a rise of blood pressure

Table 2 Effect of 15 min perfusion of ventricular system (lateral ventricle to aqueduct) with agents acting on adrenoceptors

Drug (concentration per ml)	*Drug pretreatment (concentration per ml)*	*No. of expts*	*Change in blood pressure (mmHg ± s.e.)*	*Change in heart rate (beats/min ± s.e.)*
Adrenaline (100 μg)	None	3	+18.0 ± 5.8	+17.0 ± 3.5
	Piperoxan (500 μg)	3	+24.0 ± 2.8	+10.0 ± 2.2
	Piperoxan (500 μg) + Sotalol (2.0 mg)	3	+2.1 ± 2.9	+3.3 ± 2.9
Isoprenaline (100 μg)	None	3	+10.0 ± 2.5	+20.0 ± 4.6
	Sotalol (2.0 mg)	3	+1.8 ± 2.2	+1.6 ± 2.4
Clonidine (60 μg)	None	2	−15.0	−10.0
	Piperoxan (500 μg)	2	−2.5	−2.0

Table 3 Effect of agents acting on adrenoceptors on the medullary cardiovascular loci

Drug (concentration per ml)	*Pretreatment (concentration per ml)*	*No. of expts*	*Changes in cardiovascular parameters*			
			Drug perfusion (15 min) (IV^{th} Vent. Cisterna)		*Drug superfusion (15 min) (LMPA)*	
			BP (mmHg ± s.e.)	*HR (beats/min ± s.e.)*	*BP (mmHg ± s.e.)*	*HR (beats/min ± s.e.)*
Adrenaline (100 µg)	None	10	−20.0 ± 3.3	−10.0 ± 2.1	−10.0 ± 3.5	−15.0 ± 5.0
(100 µg)	Piperoxan (500 µg)	8	+20.0 ± 3.1	+12.0 ± 2.5	+15.0 ± 5.0	+10.0 ± 2.0
(100 µg)	Piperoxan (500 µg) + Sotalol (2.0 mg)	8	+2.6 ± 2.8	+2.3 ± 3.1	+1.8 ± 2.2	+2.1 ± 2.9
Isoprenaline (100 µg)	None	4	+10.0 ± 1.9	+20.0 ± 3.8	+25.0 ± 5.0	+16.0 ± 3.9
(100 µg)	Sotalol (2.0 mg)	3	+3.3 ± 3.1	+4.8 ± 3.6	+4.2 ± 3.2	+2.4 ± 3.5
Clonidine (60 µg)	None	4	—	—	−30.0 ± 4.3	−20.0 ± 3.6
(60 µg)	Piperoxan (500 µg)	3	—	—	−1.6 ± 4.4	−3.3 ± 3.3
Noradrenaline (100 µg)	None	2	−25.0	−10.0	—	—
(100 µg)	Piperoxan (500 µg)	2	−2.5	0.0	—	—

Table 4 Cardiovascular effects of agents acting on cholinoceptors, superfused for 15 min into the medullary reticular pressor area of cat

Drugs and dose (concentration per ml)	*Pretreatment (mg/ml)*	*No. of expts*	*Mean change (at peak effect)* Early phase (1–15 min) BP (mmHg ± s.e.)	Early phase (1–15 min) HR (beats/min ± s.e.)	Late phase (15–40 min) BP (mmHg ± s.e.)	Late phase (15–40 min) HR (beats/min ± s.e.)
Acetylcholine (500 µg)	Physostigmine (1.0)	4	+36.3 ± 5.4	+30.0 ± 4.0	−33.8 ± 3.8	−10.0 ± 2.0
	Physostigmine (1.0)	3	−47.5 ± 8.2	−10.0 ± 4.2	+33.3 ± 7.8	+39.6 ± 6.2
	Ethylbenztropine (2.0)	4	+26.7 ± 2.3	+20.2 ± 3.4	+15.2 ± 2.8	+10.3 ± 2.1
	Chlorisondamine (2.0)	3	−17.5 ± 2.3	−10.2 ± 2.2	−32.5 ± 7.6	−18.1 ± 4.2
	Ethylbenztropine (2.0) + Chlorisondamine (2.0)	3	—	—	+1.6 ± 4.4	+3.3 ± 4.1
Carbachol (500 µg)	None	5	+22.6 ± 2.1	+12.1 ± 2.2	−25.3 ± 2.8	−40.8 ± 5.6
	None	6	−20.2 ± 2.1	−34.3 ± 4.3	−32.4 ± 5.8	−55.2 ± 9.3
	Chlorisondamine (2.0)	3	−16.3 ± 1.8	−28.6 ± 3.2	−26.2 ± 3.4	−52.8 ± 8.3
	Chlorisondamine (2.0) + Ethylbenztropine (2.0)	3	—	—	+3.3 ± 4.4	−4.6 ± 3.8
Nicotine (250 µg)	None	4	+70.4 ± 9.8	+54.6 ± 5.3	−52.3 ± 4.8	−38.2 ± 4.3
	Ethylbenztropine (2.0)	3	+83.2 ± 10.3	+50.4 ± 4.8	−49.7 ± 5.3	−40.6 ± 3.2
	Chlorisondamine (2.0)	4	−28.2 ± 4.2	−22.3 ± 3.2	−41.6 ± 7.7	−35.5 ± 4.9
	Piperoxan (1.0)	3	+75.8 ± 7.3	+30.3 ± 3.6	+15.3 ± 3.4	+10.2 ± 2.7
	Piperoxan (1.0) + Chlorisondamine (2.0)	4	—	—	+2.5 ± 4.3	+2.5 ± 3.1
	6-Hydroxydopamine (25)	2	+60.0	+50.0	−5.0	0.0
	Chlorisondamine (2.0)	2	—	—	−2.5	0.0
DMPP (500 µg)	None	3	+30.3 ± 4.6	+10.3 ± 4.3	+38.4 ± 5.3	+15.6 ± 5.4
	Chlorisondamine (2.0)	3	—	—	+1.6 ± 3.3	0.0
Oxotremorine (200 µg)	None	5	−28.3 ± 2.8	−42.4 ± 7.8	−20.4 ± 3.7	−32.2 ± 4.9
	Ethylbenztropine (2.0)	3	—	—	+1.6 ± 4.4	0.0
Pilocarpine (5.0 mg)	None	5	−33.4 ± 6.8	−18.6 ± 3.4	−27.2 ± 3.4	−10.3 ± 4.9
	Ethylbenztropine (2.0)	3	—	—	−3.3 ± 1.6	−3.3 ± 3.3

and heart rate. Superfusion of piperoxan (1.0 mg/ml) failed to antagonize the cardiovascular effects of nicotine and carbachol but they were antagonized by prior superfusion of sotalol (2.0 mg/ml) or chlorisondamine (2.0 mg/ml) (see Table 1).

Superfusion of the PH with the muscarinic agonists, pilocarpine (5.0–10.0 mg/ml) or oxotremorine (200–500 μg/ml) failed to elicit any cardiovascular effects.

Effect of autonomic agents on the lateral medullary reticular pressor area (LMPA)

Adrenoceptor stimulants. The results of the study are summarized in Table 3.

Superfusion of LMPA with adrenaline (100 μg/ml) or its perfusion from the IVth ventricle to the cisterna magna was found to induce a fall in blood pressure (10.0 ± 3.5 and 20.0 ± 3.3 mmHg, respectively) and heart rate (15.0 ± 5.0 and 10.0 ± 2.1 beats/min, respectively). Prior superfusion with piperoxan (500 μg/ml) in LMPA or perfusion into the IVth ventricle was found to convert the depressor effect and bradycardia induced by adrenaline into a pressor response and tachycardia. Subsequent treatment with sotalol (2.0 mg/ml) or propranolol (1.0 mg/ml) effectively blocked these excitatory responses to adrenaline.

Perfusion of isoprenaline (100 μg/ml) in the IVth ventricle or its superfusion in LMPA elicited a rise in blood pressure (10.0 ± 1.9 and 25.0 ± 5.0 mmHg, respectively) and heart rate (20.0 ± 3.8 and 16.0 ± 3.9 beats/min, respectively). These effects could not be modified by prior piperoxan treatment but they were completely blocked by sotalol or propranolol.

Superfusion of clonidine (60 μg/ml) in LMPA or perfusion of noradrenaline (100 μg/ml: in the IVth ventricle elicited a decrease in blood pressure (30.0 ± 4.3 and 25.0 mmHg, respectively) and heart rate (20.0 ± 3.6 and 10.0 beats/min, respectively); these effects were blocked by prior central piperoxan treatment (500 μg/ml).

Cholinoceptor stimulants. Table 4 summarizes the results obtained by superfusion of cholinomimetic agents in the LMPA.

Acetylcholine (500 μg/ml) superfusion elicited a biphasic cardiovascular response in atropine methyl nitrate (1.0 mg/kg i.v.) and physostigmine (1.0 μg/ml superfusion) treated cats. In 4 cats, there was an initial rise in blood pressure (36.3 ± 5.4 mmHg) followed by a delayed fall in blood pressure (33.8 ± 3.8 mmHg). These responses were associated with tachycardia and bradycardia respectively. In 3 animals, there was an initial hypotension (47.5 ± 8.2 mmHg) and bradycardia (10.0 ± 4.2 beats/min) followed by hypertension (33.3 ± 7.8 mmHg) and tachycardia (39.6 ± 6.2 beats/minute). The onset of action of acetylcholine was within 2 minutes. The initial phase lasted for approximately 15 min, and the total duration of action was about 40 minutes. Ethylbenztropine (2.0 mg/ml) pretreatment was found to convert the biphasic response into a pure pressor response and tachycardia; subsequent chlorisondamine treatment blocked the pressor-tachycardia.

Superfusion of carbachol (500 μg/ml) produced a biphasic response, pressor-tachycardia followed by depressor-bradycardia in 5 cats. Prior superfusion with chlorisondamine (2.0 mg/ml) in these animals blocked the excitatory phase of the carbachol response. In 6 cats carbachol elicited only a depressor-bradycardia response which was blocked by prior superfusion with ethylbenztropine (2.0 mg/ml) in both normal and chlorisondamine pretreated cats.

Nicotine (250 μg/ml) superfusion into LMPA produced a biphasic response consisting of an initial increase in blood pressure (70.4 ± 9.8 mmHg) and heart rate (54.6 ± 5.3 beats/min) followed by a depressor response (52.3 ± 4.8 mmHg) and bradycardia (38.2 ± 4.3 beats/minute). Prior superfusion of piperoxan (1.0 mg/ml) or 6-hydroxydopamine (25.0 mg over a period of 3 h) abolished the delayed depressor-bradycardia while chlorisondamine (2.0 mg/ml) superfusion completely abolished the early pressor and tachycardia response. It should be pointed out that the central nicotine response was unaltered after ethylbenztropine treatment.

Superfusion of two muscarinic agonists, pilocarpine (5.0 mg/ml) or oxotremorine (200 μg/ml) into LMPA produced only hypotension and bradycardia; prior superfusion with ethylbenztropine (2.0 mg/ml) completely blocked these effects.

Superfusion of a pure nicotinic agent, dimethyl phenyl piperazinium (DMPP 500 μg/ml) produced only a rise in blood pressure and heart rate which could be blocked by prior superfusion of chlorisondamine (2.0 mg/ml).

Effect of autonomic agents on the cardiovascular loci in the spinal cord

The effects of autonomic drugs injected intrathecally (i.th.) were studied on the vasomotor response elicited by compression of the spinal cord (SCVR) and the results are shown in Table 5.

Adrenoceptor stimulants. Intrathecal injections of adrenaline (10 μg) or isoprenaline (50 μg) facilitated SCVR in cats. The excitatory effects of adrenaline and isoprenaline on SCVR were blocked by prior intrathecal treatment with propranolol (1.0 mg) but were unaltered by piperoxan (100 μg). In contrast, clonidine (2 μg i.th.) inhibited SCVR and this inhibition was blocked by piperoxan (100 μg i.th.).

Cholinoceptor stimulants. Intrathecal administration of acetylcholine (10 μg), carbachol (50 μg) or nicotine (25 μg) enhanced SCVR. In cats pretreated with physostigmine (200 μg i.th.) acetylcholine-induced enhancement of SCVR was potentiated. The enhancement of SCVR induced by these cholinomimetic drugs was not altered by ethylbenztropine (500 μg i.th.) pretreatment but was completely blocked by intrathecal chlorisondamine (500 μg).

Discussion

Suitable techniques were employed in the present study to localize drugs in the areas of the posterior hypothalamus, the medullary lateral reticular pressor area and the spinal autonomic loci in order to determine the role of the adrenoceptors and the cholinoceptors of these areas in cardiovascular control. From our results it can be stated that the central α-adrenoceptors all along the neuroaxis are concerned with hypotension and bradycardia. Localization of an α-agonist, clonidine in the region of the posterior hypothalamus induced hypotension and bradycardia and these effects were antagonized by the central administration of piperoxan, an α-adrenoceptor blocking agent (Schmitt, Schmitt & Fenard, 1971; Bhargava, 1975a). The presence of inhibitory α-adrenoceptors in the rat anterior hypothalamus has been shown by the use of noradrenaline and phenylephrine as agonists and phentolamine as an antagonist (Struyker Boudier, Smeets, Brouwer & van Rossum, 1974). It appears that the α-adrenoceptors subserving inhibitory cardiovascular function exist in the anterior as well as posterior hypothalamus.

Inhibitory α-adrenoceptors have been reported in the nucleus tractus solitarius (Haeusler & Finch, 1972; De Jong, 1974; Sinha, Tangri, Bhargava & Schmitt, 1975) and the motor nucleus of the vagus (Sinha *et al.*, 1975). The results of the present study show the presence of inhibitory α-adrenoceptors in the medullary lateral reticular pressor area, since localization of clonidine or noradrenaline in this region elicited hypotension and bradycardia which

Table 5 Effect of agents acting on adrenoceptors or cholinoceptors on spinal compression vasomotor response

Drug (μg i.th.)	*Drug pretreatment (i.th.)*	*No. of expts*	*% change in SCVR ± s.e.*
Adrenaline (10)	None	5	+51.0 ± 7.5
	Piperoxan (100 μg)	3	+62.0 ± 10.8
	Propranolol (1.0 mg)	2	No change
Isoprenaline (50)	None	4	+69.1 ± 15.0
	Propranolol (1.0 mg)	4	No change
Clonidine (2)	None	4	−44.0 ± 3.6
	Piperoxan (100 μg)	4	No change
Acetylcholine (10)	None	3	+28.2
	Physostigmine (200 μg)	2	+48.5
	Ethylbenztropine (500 μg)	2	+31.3
	Chlorisondamine (500 μg)	2	No change
Carbachol (50)	None	2	+36.5
	Ethylbenztropine (500 μg)	2	+68.3
	Chlorisondamine (500 μg)	2	−32.5
Nicotine (25)	None	2	+39.7
	Chlorisondamine (500 μg)	2	−29.2

were blocked by piperoxan. Similar inhibitory α-adrenoceptors seem to be located in the spinal cord.

In contrast to the α-adrenoceptors, the β-adrenoceptors seem to subserve a facilitatory function in the central control of the cardiovascular system. Activation of the β-receptors in the posterior hypothalamus, medullary reticular pressor area and the spinal autonomic loci resulted in tachycardia and hypertension and these effects were blocked by the β-blockers, sotalol and propranolol. A facilitatory role for the hypothalamic β-adrenoceptor in cardio-acceleration, hypertension and arrhythmia has been described (Bhargava & Srivastava, 1972; Saxena & Bhargava, 1974; 1975). Activation of β-adrenoceptors of the posterior hypothalamic neurones has been held responsible for the centrogenic release of adrenaline from the adrenals (Bhargava, 1972; Bhargava & Srivastava, 1972).

Both adrenaline and noradrenaline neurones have been identified in central cardiovascular loci (Hokfelt, Fuxe, Goldstein & Johansson, 1974; Fuxe, Hokfelt, Goldstein, Jonsson, Lidbrink, Ljungdahl & Sachs, 1975). These central catecholaminergic neurones seem to be intimately concerned with disorders of the blood pressure (Saavedra, Grobecker & Axelrod, 1976; Black & Petito, 1976). It is our contention that adrenaline releasing neurones subserve central β-adrenoceptors which are concerned with hypertension and cardiac arrhythmia and that noradrenaline releasing neurones subserve central α-adrenoceptors which are inhibitory for cardiovascular control. There appears to be a preponderance of β-adrenoceptors in the posterior hypothalamus and the spinal autonomic loci. In the medullary region, however, the α-adrenoceptors seem to predominate. Thus central excitatory adrenergic mechanisms exist at the hypothalamic and spinal levels and the inhibitory adrenergic mechanisms of cardiovascular control lie at the brain stem level.

Table 6 Functional role of central adrenoceptors and cholinoceptors in cardiovascular responses

	Adrenoceptors		*Cholinoceptors*	
	α	β	*n*	*m*
Hypothalamus (posterior)	−	++	++	Absent
Medulla (reticular pressor area)	−−	+	+	−
Spinal autonomic loci	−	++	++	??

n = nicotonic cholinoceptors; m = muscarinic cholinoceptors.
+ = Excitatory response; − = Inhibitory response.

Table 6 summarizes the functional role of central adrenoceptors and cholinoceptors in cardiovascular control.

The nicotinic (n) receptors, all along the neuroaxis, are concerned with rise of blood pressure and tachycardia. In this respect they seem to function like β-adrenoceptors. The muscarinic (m) receptors on the other hand, like the α-adrenoceptors, seem to be inhibitory. There are no m-receptors in the posterior hypothalamus. A preliminary report on the role of these cholinoceptors in cardiovascular control has been presented (Bhargava, 1975b).

Studies with nicotine provide proof of a link between cholinergic and adrenergic mechanisms. Nicotine releases catecholamines in brain (Westfall, Fleming, Fudger & Clark, 1967). The release of catecholamines in the hypothalamus induced a rise in blood pressure and tachycardia which were blocked by sotalol and similar release by nicotine in the medullary region induced hypotension and bradycardia which were blocked by piperoxan or prior depletion of catecholamines by 6-hydroxydopamine. These studies provide further support for the predominance of β-adrenoceptor activity at the hypothalamic level and α-adrenoceptor activity at the medullary level.

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