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Effect of Dopamine Receptor Activation on Ganglionic Transmission and cyclic AMP Levels in the Stellate Ganglia and Renal Arteries of the Dog[1]

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ABSTRACT

By using selective dopamine (DA) receptor agonists and antagonists, we have demonstrated previously the presence of DA-2- and DA-1-like DA receptors in the stellate ganglia of the dog. Activation of either DA-2- or DA-1-like receptors by quinpirole or fenoldopam, respectively, leads to inhibition of ganglionic transmission. In the present study we have examined the involvement of DA receptor subtypes in the action of DA on ganglionic transmission. Inasmuch as stimulation of DA receptors is linked to the activation (DA-1) or inhibition (DA-2) of the enzyme adenylate cyclase, we have also measured the accumulation of cyclic AMP (cAMP) for biochemical characterization of ganglionic DA receptors. In isolated stellate ganglia treated with phentolamine and propranolol, DA caused concentration-dependent inhibition of ganglionic transmission as evidenced by reductions in the amplitude of the evoked postganglionic compound action potentials. The inhibitory effect of DA on ganglionic transmission was antagonized by both the DA-1 receptor antagonist, *R*-sulpiride, and the DA-2 receptor antagonist, *S*-sulpiride. However, the more potent and selective DA-1 receptor antagonist, SCH-23390, failed to antagonize the DA-induced inhibition of ganglionic transmission. Isolated stellate ganglia were also utilized for the measurement of cAMP. Neither DA nor the selective DA-1 receptor agonist, fenoldopam, caused any significant changes in cAMP, suggesting the lack of an adenylate cyclase-linked DA-1 receptor in the ganglia. On the other hand, *beta* adrenoceptor activation by isoproterenol produced a 3-fold increase in cAMP content of the stellate ganglia. The DA-2 receptor agonist, quinpirole, caused a moderate but significant inhibition of adenylate cyclase activity, an action that was blocked by the DA-2 receptor antagonist *S*-sulpiride. In vascular smooth muscle where the presence of a DA-1 receptor is well established, DA and fenoldopam produced significant increases in cAMP in dog renal arteries. The DA and fenoldopam-induced elevations of cAMP were mediated by the DA-1 receptor because of the inhibition of this increase by selective DA-1 receptor antagonists *R*-sulpiride and SCH-23390. These findings show the presence of two distinct subtypes of DA receptors in stellate ganglia. The ganglionic DA-2 receptor is similar to the presynaptic DA-2 receptor on sympathetic nerve terminal, and to the D-2 receptor on the mammotrophs of the anterior pituitary with regard to its ability to inhibit cAMP. However, the other subtype of ganglionic DA receptor appears to be different from the vascular DA-1 receptor based on the lack of association of ganglionic DA receptor to the enzyme adenylate cyclase and its insensitivity to blockade by SCH-23390.

The existence of two distinct subtypes of peripheral DA receptors has now been clearly established. Peripheral DA-1 and DA-2 receptors are shown to have different localizations, have different structural requirements for agonists and antagonists and to mediate different physiological functions (Lokhandwala and Barrett, 1982; Goldberg and Kohli, 1983). The recent development of selective DA receptor agonists and antagonists have further helped in the characterization of peripheral DA receptors into DA-1 and DA-2 subtypes (Hahn, 1984; Berkowitz *et al.*, 1984; Kaiser and Jain, 1985).

Unlike vascular DA receptors and DA receptors on sympathetic nerve terminals, little is known concerning the presence and subtype of specific ganglionic DA receptors, although earlier studies have shown an action of DA at the level of the sympathetic ganglia (Libet and Tosaka, 1970; Lins and Willems, 1974; Horn *et al.*, 1982). More recently, there have been studies conducted by us as well as others to determine the actions of DA-1 and DA-2 receptor agonists on ganglionic transmission (Shebuski *et al.*, 1985; Sabouni *et al.*, 1986; Lokhandwala *et al.*, 1985). *In vivo* and *in vitro* studies from our laboratory have revealed the existence of two DA receptor subtypes in stellate ganglion of the dog. Although one subtype could be classified under the current terminology as a DA-2 receptor, the other subtype of DA receptor could not be termed a typical DA-1 receptor (Sabouni *et al.*, 1986).

Inasmuch as DA can influence ganglionic transmission by

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ABBREVIATIONS: DA, dopamine; cAMP, cyclic AMP.

stimulating DA-1 and DA-2 receptors (Lokhandwala and Barrett, 1982) as well as *alpha* and *beta* adrenoceptors (DeGroat and Volle, 1966a,b; Quenzer *et al.*, 1979), we have studied the effect of DA on ganglionic transmission after blockade of *alpha* and *beta* adrenoceptors, to examine the involvement of DA-receptor subtype(s) in the action of DA. Moreover, inasmuch as D-1 or DA-1 receptor activation has been associated with increases in cAMP accumulation (Kebabian and Calne, 1979; Stoof and Kebabian, 1984), whereas D-2 or DA-2 receptor activation has been linked to a decrease in adenylate cyclase activity (Kebabian and Calne, 1979; Stoof and Kebabian, 1984), we utilized this biochemical approach in the present investigation to further characterize ganglionic DA receptor(s).

Methods

Mongrel dogs of either sex were anesthetized with sodium pentobarbital (35 mg/kg i.v.) and were respired with room air after endotracheal intubation using a Harvard respirator. A right thoracotomy was performed at the second intercostal space and the stellate ganglion was exposed. After ligation and sectioning of the pre- and postganglionic nerves, the ganglion was removed quickly and desheathed carefully under a microscope while maintained in cold, oxygenated (5% CO_2-95% O_2) Locke's solution (pH = 7.4) containing (millimolar): NaCl, 136; KCl, 5.6; $CaCl_2$, 2.2; $MgCl_2$, 1.2; NaH_2PO_4, 1.2; $NaHCO_3$, 20.0; and glucose, 11.0.

Electrophysiological studies. The ganglia were immersed in Locke's solution in a constant temperature (37°C) chamber with the pre- and postganglionic (inferior cardiac) nerves drawn into stimulating and recording suction electrodes. The preganglionic nerve was stimulated regularly supramaximally by square-wave pulses (0.5 msec duration at 0.3 Hz). Postganglionic compound action potentials were recorded using a capacity-coupled preamplifier, and the amplified potentials were displayed on an oscilloscope and permanent records were made on photographic film.

Ganglia were allowed to equilibrate in Locke's solution containing phentolamine (10^{-5} M) and propranolol (10^{-5} M) for 30 min or until the action potentials were stable. DA was added to the perfusion fluid and changes in the amplitude of the action potentials were used as indices of effects on ganglionic transmission. After recording five steady-state "control" action potentials, concentration-response relationships were obtained by testing increasing cumulative concentrations of DA on the action potential. Each new concentration was left in the bath for 5 min during which a new steady state was reached before recording of five consecutive action potentials. When all concentrations were tested, DA was then removed by repeated washing (5 times) with Locke's solution. The action potential was allowed to recover (20–40 min) before an antagonist was added and the series of concentrations of DA were repeated in the presence of the antagonist. The effect of DA on ganglionic transmission was expressed as the percentage of change in the amplitude of the action potential.

cAMP Assay

Stellate ganglia. Ganglia were removed and maintained in Locke's solution containing theophylline (10 mM). After desheathing, the pre- and postganglionic nerves were removed and an equilibration period of 30 min at room temperature was allowed. The ganglia were then incubated at 37°C for 15 min in beakers containing the test solutions. After the incubation procedure the ganglia were homogenized in 600 μl of 0.3 N perchloric acid using polytron homogenizer. After centrifugation at 12,000 × *g* for 10 min, the supernatant was neutralized with 3 M $KHCO_3$ (50 μl) and spun at 1000 × *g* for 5 min. The supernatant was assayed for cAMP in duplicate samples using cAMP assay kit from Amersham Corporation (Arlington Heights, IL). The assay is based on the competition between unlabeled cAMP and a fixed quantity of tritium-labeled cAMP for binding to a protein which has a high specificity for cAMP. The amount of labeled cAMP-protein complex formed is related inversely to the amount of unlabeled cAMP present in the assay. The concentration of cAMP in the unknown is determined by comparison with a linear standard curve. Samples from the homogenate before the first period of centrifugation were assayed for protein content by the method of Lowry *et al.* (1951) using bovine serum albumin as a standard.

Renal arteries. The renal arteries were excised quickly from the dogs immediately after the removal of the stellate ganglia. The arteries were equilibrated (30 min) at room temperature and homogenized in Krebs-Ringer bicarbonate buffer containing theophylline (10 mM). The homogenate was apportioned into tubes and incubated for 20 min with or without drugs at 37°C under adequate oxygenation. The homogenates were then centrifuged at 15000 × *g* for 10 min and the pellets were discarded. From each tube, 50 μl of the supernatant was taken and assayed for cAMP as described above and the protein content was determined (Lowry *et al.*, 1951).

Changes were analyzed by paired *t* test in the absence and in the presence of the antagonist. Statistical significance was assigned at $P < .05$.

Drugs used. Fenoldopam (Smith Kline and French Laboratories, Philadelphia, PA), quinpirole (Eli Lilly and Co., Indianapolis, IN), DA (Sigma Chemical Co., St. Louis, MO), *R*- and *S*-sulpiride (Ravizza, S. P. A. Milan, Italy), phentolamine (Ciba Pharmaceutical Co., Summit, NJ), propranolol (Ayerst Laboratories, Princeton, NJ) and SCH-23390 (Schering Corporation, Bloomfield, NJ).

Results

Effect of DA on ganglionic transmission. In the presence of both phentolamine (10^{-5} M) and propranolol (10^{-5} M), DA caused concentration-dependent decreases in the amplitude of the postganglionic compound action potential elicited by preganglionic stimulation. At the highest concentration used (3.55×10^{-4} M), the action potential amplitude was reduced by approximately 70% (fig. 1). The inhibitory action of DA on ganglionic transmission was reversible and the amplitude of the compound action potential returned to the control value within 20 to 40 min after removal of the drug.

Inasmuch as DA can activate DA-1 as well as DA-2 receptors, preferential DA receptor antagonists were used to assess the contribution of each DA receptor subtype to the inhibitory action of DA. After obtaining the responses to DA, ganglia were treated with *R*-sulpiride (10^{-5} M), *S*-sulpiride (10^{-5} M) or SCH-23390 (10^{-5} M) in separate groups of experiments. The inhibitory effects of DA on ganglionic transmission were antagonized significantly at all concentrations tested after pretreatment with the DA-1 receptor antagonist *R*-sulpiride and the DA-2 receptor antagonist *S*-sulpiride (figs. 2 and 3). However, pretreatment with the vascular DA-1 receptor antagonist, SCH-23390, did not alter the inhibition of ganglionic transmission produced by DA (fig. 4). It should be noted that, at concentra-

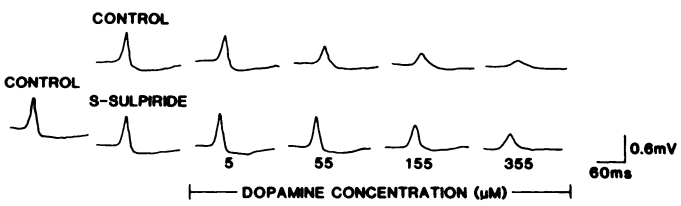

Fig. 1. Effect of DA on the compound action potential recorded from an isolated stellate ganglion pretreated with phentolamine and propranolol. After recording control responses, cumulative concentrations of DA were added to the bath (upper traces). The drug was then removed by repeated washing and the ganglion was allowed to recover before addition of *S*-sulpiride (10^{-5} M). The same series of DA concentrations were added in the presence of this antagonist (lower traces).

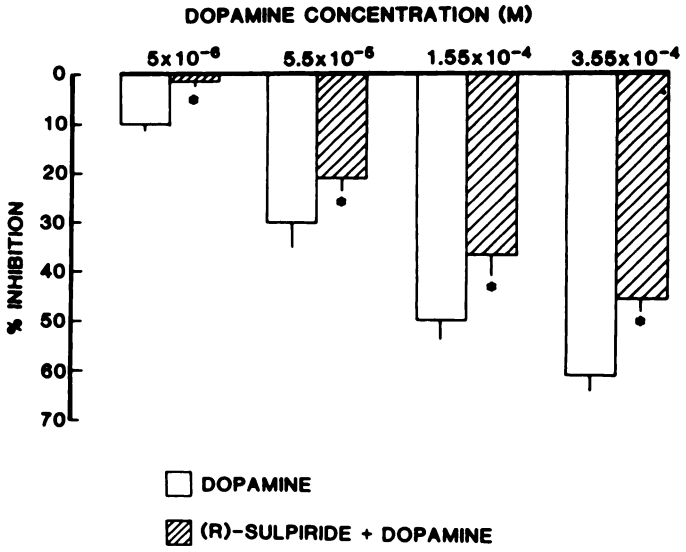

Fig. 2. Effect of DA on the compound action potential recorded from the stellate ganglia pretreated with phentolamine (10^{-5} M) and propranolol (10^{-5} M). *R*-sulpiride (10^{-5} M) antagonized significantly the inhibitory action of DA on ganglionic transmission ($N = 5$, $^*P < .05$).

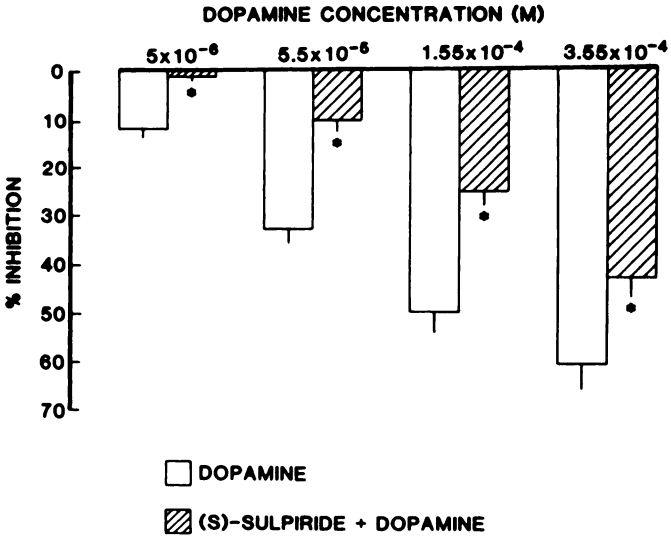

Fig. 3. Effect of DA on the compound action potential recorded from the stellate ganglia pretreated with phentolamine and propranolol. *S*-sulpiride (10^{-5} M) antagonized significantly the inhibitory action of DA on ganglionic transmission ($N = 5$, $^*P < .05$).

tions 100 times lower than what was used in this study, SCH-23390 is shown to antagonize renal vasodilatory action of fenoldopam in the isolated perfused rat kidney (Lokhandwala and Steenberg, 1984).

cAMP in ganglia. The control value of cAMP in the stellate ganglia at the end of the incubation period was 4.87 ± 0.46 pmol of cAMP mg^{-1} of protein (wet weight). Ganglia incubated with isoproterenol (10^{-5} M) showed a 287% increase in cAMP levels, whereas incubation with DA had no effect on ganglionic cAMP (table 1). To evaluate further the effects of DA receptor activation on adenylate cyclase activity, the DA-1 and DA-2 receptor agonists, fenoldopam and quinpirole, respectively, were used. Incubation with fenoldopam (10^{-4} M) caused no significant change in cAMP from the control values. However, quinpirole (10^{-4} M) produced a small but significant decrease of 33% in ganglionic cAMP which was antagonized in the

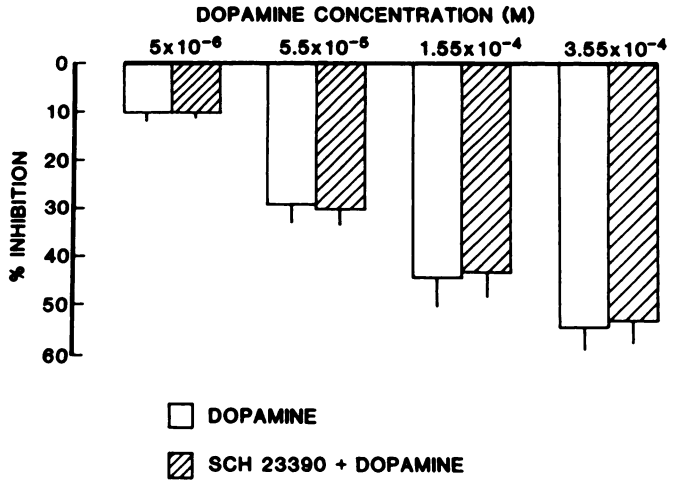

Fig. 4. Effect of DA on the compound action potential recorded from the stellate ganglia pretreated with phentolamine and propranolol. SCH-23390 (10^{-5} M) failed to antagonize the inhibitory action of DA on ganglionic transmission ($N = 5$).

TABLE 1

Content of cAMP in dog stellate ganglia treated with adrenergic and dopaminergic drugs

Ganglia were incubated for 15 min with drugs in the presence of theophylline (10 mM) at 37°C. Values given are mean ± S.E.M.; numbers in parenthesis represent number of experiments.

Drugs	cAMP	% Change in cAMP Content
	pmol mg^{-1}	
None	4.87 ± 0.46 (6)	
Isoproterenol (10^{-5} M)	18.84 ± 0.7* (3)	+287
DA (10^{-4} M)	5.50 ± 0.32 (3)	+13
Fenoldopam (10^{-4} M)	5.32 ± 0.29 (3)	+9
Quinpirole (10^{-4} M)	3.25 ± 0.09* (3)	−33
S-sulpiride (10^{-5} M) + quinpirole (10^{-4} M)	3.92 ± 0.19† (3)	−19

* Significantly different from control ($P < .05$); † significantly different from values obtained with respective agonist alone ($P < .05$).

presence of the DA-2 receptor antagonist *S*-sulpiride (10^{-5} M) (table 1). We have shown previously that the concentrations of fenoldopam and quinpirole used in this study produce significant inhibition of ganglionic transmission and *R*- and *S*-sulpiride antagonized the actions of fenoldopam and quinpirole, respectively (Sabouni *et al.*, 1986).

cAMP in renal arteries. cAMP in homogenates from dog renal arteries incubated for 15 min in Krebs-Ringer bicarbonate buffer containing 10 mM theophylline was 3.41 ± 0.15 pmol mg^{-1} of protein under control conditions (table 2). Isoproterenol treatment resulted in a 117% increase in cAMP levels and this elevation was antagonized markedly after preincubation of the homogenate with propranolol (10^{-5} M).

In contrast to the results obtained in the stellate ganglia, the cAMP content of the dog renal arteries was increased significantly by 99% when incubated with DA (10^{-4} M). The DA-induced increment in cAMP content was inhibited by the DA-1 receptor antagonists *R*-sulpiride (10^{-5} M) and SCH-23390 (10^{-5} M). Propranolol (10^{-5} M), however, did not antagonize significantly the stimulatory action of DA on vascular cAMP content (table 2). Fenoldopam (10^{-4} M) also caused a significant increase of 51% in cAMP levels although it appeared to be less potent in this manner. Preincubation with either *R*-sulpiride or with SCH-23390 attenuated markedly fenoldopam-induced

TABLE 2

Content of cAMP in dog renal arteries treated with adrenergic and dopaminergic drugs

Arterial homogenates were incubated for 15 min with drugs in the presence of theophylline (10 mM) at 37°C. Values given are mean ± S.E.M.; numbers in parenthesis represent number of experiments.

Drugs	cAMP	% Change in cAMP Content
	pmol mg^{-1} protein	
None	3.41 ± 0.15 (12)	
Isoproterenol (10^{-5} M)	7.39 ± 0.60* (6)	+117
Propranolol (10^{-5} M) + isoproterenol (10^{-5} M)	3.73 ± 0.14† (5)	+9
DA (10^{-4} M)	6.81 ± 0.82* (6)	+99
Propranolol (10^{-5} M) + DA (10^{-4} M)	5.48 ± 0.15* (5)	+61
R-sulpiride (10^{-5} M) + DA (10^{-4} M)	3.54 ± 0.55† (5)	+4
SCH-23390 (10^{-5} M) + DA (10^{-4} M)	3.00 ± 0.34† (5)	−12
Fenoldopam (10^{-4} M)	5.15 ± 0.39* (6)	+51
Propranolol (10^{-5} M) + fenoldopam (10^{-4} M)	4.75 ± 0.12* (5)	+39
R-sulpiride (10^{-5} M) + fenoldopam (10^{-4} M)	3.38 ± 0.71† (5)	−1
SCH-23390 (10^{-5} M) + fenoldopam (10^{-4} M)	2.89 ± 0.28† (5)	−15

* Significantly different from control ($P < .05$); † significantly different from values obtained with respective agonist alone ($P < .05$).

elevations in cAMP, whereas propranolol did not alter this action (table 2).

Discussion

Data from the present study indicate that DA inhibits sympathetic ganglionic transmission in the dog stellate ganglia by stimulating two distinct DA receptor subtypes. They confirm and extend our previous studies on the canine stellate ganglia which showed that fenoldopam, a selective DA-1 receptor agonist, and quinpirole, a selective DA-2 receptor agonist, produced inhibition of ganglionic transmission by activating two distinct subtypes of DA receptors (Sabouni *et al.*, 1986). Furthermore, biochemical experiments from the present study provide additional evidence to support the novel finding that although ganglionic DA receptor activated by quinpirole is similar to the presynaptic DA-2 receptor, the other subtype of ganglionic DA receptor activated by both DA and fenoldopam is probably different from the vascular DA-1 receptor as will be discussed in the following sections.

Effect of DA on transmission in the stellate ganglia. In the isolated ganglia, DA caused a concentration-dependent inhibition of ganglionic transmission as evidenced from the decreases in amplitude of the evoked postganglionic compound action potential. Because these electrophysiological experiments with DA were performed in the presence of phentolamine and propranolol, the inhibitory effect of DA on ganglionic transmission in the presence of these antagonists indicates the involvement of specific DA receptors distinct from adrenergic receptors of the ganglia. Although it has been shown by previous *in vivo* and *in vitro* studies that DA exerts an inhibitory action on synaptic transmission in sympathetic ganglia (Horn *et al.*, 1982; Kushiku *et al.*, 1980; Quenzer *et al.*, 1979), this is the first electrophysiological investigation which demonstrates the involvement of DA receptors in the inhibitory action of DA in canine stellate ganglia. By using fenoldopam and quinpirole as preferential DA-1 and DA-2 receptor agonists (Ackerman *et al.*, 1983; Hahn 1984; Lokhandwala *et al.*, 1985), we have shown recently the presence of two DA receptor subtypes in the stellate ganglia. Activation of these receptors suppressed ganglionic transmission under *in vivo* and *in vitro* conditions (Sabouni *et al.*, 1986). To determine the relative involvement of DA receptor subtypes in the ganglionic actions of DA, similar electrophysiological experiments were carried out in the present study with DA. The ability of DA to activate both DA-1 and DA-2 receptors (Lokhandwala and Barrett, 1982) prompted us to use the selective DA receptor antagonists to analyze the action of DA.

That the inhibitory effect of DA could be antagonized by both the DA-1 receptor antagonist, *R*-sulpiride, and the DA-2 receptor antagonist, *S*-sulpiride, suggests the involvement of both of these receptor subtypes in the ganglionic action of DA. It should be noted that the concentrations of R- and S-sulpiride used in the present study were found to be effective in preferentially antagonizing the inhibitory actions of fenoldopam and quinpirole, respectively, on ganglionic transmission (Sabouni *et al.*, 1986). However, consistent with our previous work (Sabouni *et al.*, 1986), we again noted the failure of the selective and potent vascular DA-1 receptor antagonist SCH-23390 to antagonize the action of DA on the stellate ganglia. Similar observations were also reported in earlier studies from our laboratory showing the inability of SCH-23390 to antagonize the inhibitory action of fenoldopam (SKF-82526) on transmission in the fifth lumbar vertebral ganglion of the dog under *in vitro* as well as *in vivo* conditions (Lokhandwala *et al.*, 1985; Lokhandwala and Sabouni, 1985).

Changes in ganglionic and vascular cAMP in response to DA, fenoldopam and quinpirole. Elevations in cAMP levels have been reported to be associated with activation of D-1 or DA-1 receptor subtypes (Kebabian and Calne, 1979; Nomura *et al.*, 1984; Goldberg and Kohli, 1983). Conversely, those receptors designated as D-2 or DA-2 in many cases have been linked to inhibition of the enzyme adenylate cyclase (Kebabian and Calne, 1979; Stoof and Kebabian, 1984; Missale *et al.*, 1985). In dog renal arteries, isoproterenol, DA and fenoldopam caused stimulation of adenylate cyclase activity as evidenced by the increase in cAMP contents after treatments with these agonists, whereas stimulation of ganglionic adenylate cyclase occurred only in response to isoproterenol. In accordance with earlier studies (Murthy *et al.*, 1976; Amenta *et al.*, 1984), our data show that DA produces elevation of cyclic AMP content in dog renal artery. Furthermore, the selective DA-1 receptor agonist, fenoldopam, also caused a significant increase in arterial cAMP. The ability of the DA-1 receptor antagonists *R*-sulpiride and SCH-23390 to antagonize these effects of DA and fenoldopam supports previous suggestions that activation of vascular DA-1 receptors indeed leads to increased synthesis of intracellular cAMP. It should be noted that fenoldopam is shown to produce renal vasodilation (Hahn *et al.*, 1982; Lokhandwala and Steenberg, 1984), and our results now show that this action may result from activation of a DA-1 receptor sensitive adenylate cyclase and consequent increase in intracellular levels of cAMP.

The link between activation of *beta* adrenoceptors and stimulation of the enzyme adenylate cyclase has been documented and isoproterenol has been shown to increase vascular cAMP content (Trinter *et al.*, 1971; Murthy *et al.*, 1976). That isoproterenol increased significantly vascular cAMP in our preparation and the ability of propranolol to antagonize this

increase once again suggests the involvement of *beta* adrenoceptors and provides support for the validity of our system. Furthermore, the failure of propranolol to antagonize the stimulatory effects of DA and fenoldopam on adenylate cyclase indicates that the actions of these two agonists did not result from *beta* adrenoceptor activation, but were indeed due to activation of specific DA-1 receptors in the vascular smooth muscle.

In accordance with earlier work on rat, cat and rabbit sympathetic ganglia (Quenzer *et al.*, 1979; Williams *et al.*, 1975; Kalix *et al.*, 1974), we have demonstrated that DA lacks the ability to stimulate adenylate cyclase in dog stellate ganglia. Isoproterenol, nevertheless, produced marked increase in ganglionic cAMP indicating the presence of cyclase-linked *beta* adrenoreceptors in the stellate ganglia. Similar observations have been made by others in the rat superior cervical ganglia (Quenzer *et al.*, 1979; Volle *et al.*, 1982). In addition to DA, the DA-1 receptor agonist fenoldopam also did not cause any significant changes in the ganglionic cAMP. Therefore, it is apparent that, whereas cAMP is involved in DA-1 receptor-mediated vascular relaxation and can be used as the biochemical index for DA-1 receptor activation, the inhibition of ganglionic transmission produced by DA and fenoldopam is not associated with an increase in cAMP. These results would seem to suggest that, unlike the vascular DA-1 receptor, the DA receptor activated by DA and fenoldopam in the stellate ganglia is not adenylate cyclase-linked, and is not sensitive to blockade by the selective DA-1 receptor antagonist, SCH-23390. These two differences, namely the biochemical characteristics and the effect of SCH-23390, between the vascular DA-1 and the ganglionic DA receptor suggest that these two receptors may indeed be different, although additional studies with more selective DA-1 receptor agonists and antagonists are required before postulating a separate subtype of ganglionic DA receptor.

A recent study has shown that activation of a peripheral DA-2 receptor is associated with the inhibition of adenylate cyclase activity because DA caused both increases and decreases in adrenal cortex cAMP *via* activation of D-1 and D-2 receptors, respectively (Missale *et al.*, 1985). Because our electrophysiological experiments showed that DA-2 receptors are present in dog stellate ganglia (Sabouni *et al.*, 1986), the presence of these receptors was investigated further utilizing this biochemical approach. The finding that the DA-2 receptor agonist, quinpirole, caused a significant decrease in ganglionic cAMP content and the ability of the DA-2 receptor antagonist *S*-sulpiride to antagonize the inhibitory action of quinpirole confirms the existence of DA-2 receptors in the stellate ganglia of the dog. This ganglionic DA-2 receptor is similar to peripheral presynaptic DA-2 receptor and the central D-2 receptor present in the anterior pituitary gland.

The results of the present study and our previous study (Sabouni *et al.*, 1986) have shown that two DA receptor subtypes are present in dog stellate ganglia. Biochemical and electrophysiological investigations indicate the existence of a typical DA-2 receptor. Stimulation of this receptor leads to inhibition of ganglionic transmission and a decrease in cAMP, and both of these actions can be antagonized by *S*-sulpiride. On the other hand, electrophysiological and biochemical studies revealed some distinction between vascular DA-1 receptor and the other subtype of ganglionic DA receptor. Both receptors can be stimulated by DA and fenoldopam and antagonized by *R*-sulpiride. The disparity, however, lies in the failure of the potent DA-1 receptor antagonist, SCH-23390, to block the ganglionic DA receptor, and the association of the adenylate cyclase system with the vascular DA-1 but not with the ganglionic DA receptor.

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