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Effects of neurokinin A on Ca^{2+} mobilization in rat vas deferens

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Effects of neurokinin A (NKA) on Ca^{2+} mobilization in rat vas deferens were studied and compared with those of norepinephrine (NE). Epididymal and prostatic parts were dissected from the vas deferens to investigate regional differences.

Although both NKA and NE induced similar maximal contractions in each site, there was a marked difference in the sensitivity. NKA was more potent than NE in both sites. NKA-induced contractions were more strongly inhibited by nicardipine, a dihydropyridine Ca^{2+} entry blocker, or by elimination of extracellular Ca^{2+} in both sites, suggesting involvement of Ca^{2+} influx in the contraction. However, ryanodine, which interferes with the release of intracellular Ca^{2+}, abolished contractions caused by NKA in prostatic site while had no effect in epididymal site. These results suggest that NKA-induced contraction utilizes both intracellular and extracellular Ca^{2+} in prostatic site but mobilizes only extracellular Ca^{2+} in epididymal site.

NKA potentiated NE and adenosine triphosphate (ATP) component contraction of stimulation-induced contractions in prostatic site. In order to investigate a possibility of presynaptic action of NKA, the released transmitters, NE and ATP, were detected radiochemically. Measurement of radioactivity of [^{3}H]NE or [^{14}C]ATP revealed that NKA had no effect on both spontaneous and electrically evoked NE and ATP release in either site. These results clearly demonstrated that NKA had no effect on presynaptic nerve terminal.

Intracellular Ca^{2+} level was measured directly with Ca^{2+}-sensitive fluorescent dye fura-2. In both sites NKA caused more gradual and slower increase in intracellular Ca^{2+} concentration ($[Ca^{2+}]_i$) than NE. Furthermore, in epididymal site NKA induced contractions with smaller increase in $[Ca^{2+}]_i$ compared to that necessary for NE-induced contractions (Table 1). These results suggest that NKA utilizes Ca^{2+} more efficiently compared with NE and functions as a neuromodulator in rat vas deferens.

Table 1

The contractions and intracellular Ca^{2+} level induced by 10^{-4} M norepinephrine (ME) and 10^{-6} M neurokinin A (NKA) in rat vas deferens.

	Contraction (g)		Ratio of $[Ca^{2+}]_i$ (%)
	NE (10^{-4} M)	NKA (10^{-6} M)	NKA (10^{-6} M)
Epididymal	1.29±0.08	1.13±0.04	66.48±0.60 *
Prostatic	0.42±0.05	0.36±0.07	102.75±0.39

All values are given as mean±S.E.M. The ratio of Ca^{2+} level represent % of the maximal increase induced by NE (10^{-4} M) in each site of rat vas deferens. Asterisk indicates a significant difference between NE and NKA groups by Student's t-test (*: $p < 0.05$).

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Long-term administration of fluvoxamine antagonizes the inhibitory effect of neuropeptide Y but not the clonidine effect on isolated rat vas deferens

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It is widely accepted that neuropeptide Y (NPY) has a modulatory effect on noradrenergic transmission (Agnati et al., 1983). The importance of noradrenergic systems in the biochemical actions of antidepressant drugs and

biochemical basis of depression is likewise accepted. Thus, it is possible that NPY play a role in the mechanism of action of antidepressant drugs. Moreover, it has been reported that the central levels of NPY are decreased in affective disorders, and they increase parallely to recovery of the symptoms (Widerlov et al., 1988). In view of this possibility we are studied the functional interaction between a long-term treatment (10 mg/kg ip twice a day for 14 days) and acute treatment (10 mg/kg ip 12 h before experiment) with fluvoxamine (an antidepressant drug inhibitor of serotonin uptake) (FVX) and the inhibitory effect of NPY and clonidine (CND) on isolated rat vas deferens under field stimulation conditions (30 V, 0.1 Hz, width 1 msec). The results obtained show that long-term but not acute administration of FVX antagonizes this effect of NPY without affect the inhibitory actions of CND (table 1).

Table 1

Effect of long-term and acute administration of FVX on the IC_{50} of NPY and CND in isolated rat vas deferens under field stimulation conditions. (means S.E.M.). The results are expresed in nM.

	Saline 12 h	Saline 14 d	FVX 12 h	FVX 14 d
NPY	25.9±0.48	32.8±0.68	47.7±1.84	180.4±5.92 [a,b]
	(n = 9)	(n = 6)	(n = 4)	(n = 5)
CND	3.04±0.47	2.28±0.91	1.29±0.31	3.72±1.62
	(n = 10)	(n = 5)	(n = 9)	(n = 5)

[a] $p = 0.032$ versus FVX 12 h. [b] $p < 0.002$ versus saline 14 d. The statistical significance has been obtained using the Mann-Whitney U test.

These results show that the inhibitory actions of NPY on isolated rat vas deferens could be antagonized by FVX througth a modulatory action on NPY binding sites and rule out a possible implications of presynaptic alfa$_2$-adrenergic receptors.

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Characteristics of the P_2-purinoceptor- and H1-receptor mediated response in DDT_1 MF-2 vas deferens smooth muscle cells

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Presently, the relationship between cellular signalling processes is subject to excessive study. Some characteristics of these mechanisms observed upon stimulation of P_2-purinoceptors and H1-histaminic receptors on vas deferens DDT_1 MF-2 smooth muscle cells are described. Stimulation of P_2-purinoceptors by adenosine triphosphate (ATP, 10^{-4} M) activated a transient outward current and an inward current, measured in the whole cell patch clamp configuration (holding potential: −50 mV). The outward current is carried by potassium ions, while calcium- and sodium ions are involved in the inward current (Molleman et al., 1989). The potassium channels conducting the outward current are inhibited by tetraethylammonium (TEA; 20 mM), thought to block calcium regulated potassium channels and are partly sensitive to glipizide (10^{-5} M), known to interact with ATP modulated potassium channels. It was suggested recently (Den Hertog et al., 1989) that the antitrypanosomal agent suramin possesses P_2-purinoceptor antagonistic properties. Accordingly, both the inward- and outward currents observed in the presence of ATP in DDT_1 MF-2 cells were inhibited by suramin concentration dependently. Stimulation of histamin (His, 10^{-4} M) sensitive receptors