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REPORT, Y100026871, NSC: 88-2314-B-002-186-;
87-8-1 to 88-7-31
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[illegible]:

[illegible] 10^{-4} mM/100g [illegible] 61.3 ± 4.1 mmHg, [illegible]

[illegible] guanethidine (10^{-5} mM/100g), phenoxybenzamine (10^{-7} mM/100 g), prazosin (10^{-8} mM/100g), WB-4101 (10^{-8} mM/100g) [illegible] yohimbine (10^{-8} mM/100g) [illegible] (noradrenergic nerve) [illegible] α1 ([illegible] α1A) [illegible] α2 [illegible] (adrenergic receptors) [illegible]

[illegible] haloperidol (5×10^{-6} mM/100g), R(+)-SCH 23390 (10^{-8} mM/100g), domperidone (10^{-7} mM/100g) [illegible] S(-) sulpiride (5×10^{-7} mM/100g) [illegible] D1 [illegible] D2 [illegible] atropine (10^{-8} mM/100g) [illegible] (cholinergic nerve) [illegible]

[illegible] α2-[illegible] α1-[illegible] D1 [illegible] D2 [illegible]

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Investigation of Dopaminergic System on the Rat Seminal Vesicle *-in vivo* study

Abstract

Using our established animal model, mature male Wistar rats were used in this study. The maximal pressure response of the seminal vesicle was 61.3 ± 4.1 mmHg by intraarterial injection of dopamine (10^{-4} mM/100g). Pretreatment with guanethidine (10^{-5} mM/100g), phenoxybenzamine (10^{-7} mM/100 g), prazosin (10^{-8} mM/100g), WB-4101 (10^{-8} mM/100g) and yohimbine (10^{-8} mM/100g) inhibited the pressure response of seminal vesicle to exogenous dopamine significantly. This implied the involvement of noradrenergic nerve and the excitement of α1 (especial α1A) and α2 adrenergic receptors in this process. However, β adrenergic receptor was not excited. Pretreatment with haloperidol ($5x10^{-6}$ mM/100g), R(+)-SCH 23390 (10^{-8} mM/100g), domperidone (10^{-7} mM/100g)and S(-) sulpiride ($5x10^{-7}$ mM/100g) inhibited the pressure response of seminal vesicle to dopamine significantly also. D1 and D2 dopaminergic receptors were excited in this process. Pretreatment with atropine (10^{-8} mM/100g) also suppressed the pressure response indicated the involvement of cholinergic nervous systems. Cervical spinal cord trans-section decreased the pressure response induced by dopamine; this strongly suggested that CNS regulated the dopaminergic system of the rat seminal vesicle.

In conclusion, peripheral dopaminergic system existed in the rat seminal vesicle and was regulated by CNS. The exogenous dopamine induced seminal vesicle pressure response was activated via noradrenergic nerve; properly via α2 (presynaptic) and α1A (postsynaptic) adrenoreceptors, or by D1 and D2 dopaminergic receptors. The cholinergic nervous system involved in this process was possible but need to do further investigation.

Keywords: dopaminergic nervous system, seminal vesicle

Introduction

Kimura Y et al showed a positive relationship between brain dopaminergic system and ejaculation.[1] Central dopaminergic system regulates the sexual behavior has also been demonstrated on the rat, the rabbit and the dog.[2-6] Medial preoptic area and nucleus accumbens are the possible areas to control the process of ejaculation.[7-11] Sharif and Gokhale demonstrated a dose dependent contraction induced by dopamine on the isolated rat seminal vesicle.[12] A tonic and rhythmic contractions in rat vas deferentia induced by exogenous dopamine has also proved by Lafi and Leake.[13] Some studies demonstrated the presence of dopamine and its metabolites in the genital organs and spinal nerve.[14-19] Dopaminergic receptors was demonstrated on the

smooth muscle cells and the glandular tissue of seminal vesicle by autoradiographic technique.[17] Dopamine and noradrenaline co-existed in the same sympathetic neurons[20] and the dopaminergic receptors located presynaptically were also proved.[14, 21- 24] The existence of peripheral dopaminergic system in genital organs is possible. The purpose of this study is going to clarify the neurotransmission of dopaminergic system on the rat seminal vesicle.

Materials and Methods

Mature male Wistar rats (12-14 weeks) were obtained from the animal center of National Taiwan University Medical College. Rats were housed four per cage at 23 à g with a 12-h light-dark cycle (07.00-19.00 hours) and free access to food and water.
Rats were anaesthetized with pentobarbital (40 mg/kg, intraperitoneally); the experimental procedure was described previously.[25] Briefly, the trachea of the rat was intubated to maintain a patent airway, and catheter placed in the common carotid artery for continuous blood pressure monitoring. The anaesthetic agent was injected through the femoral vein. The test drugs and dopamine were administrated through a catheter placed from the femoral artery to the bifurcation of the common iliac artery. A polyethylene catheter (PE-60) filled with normal saline was placed via the tail into the main lumen of the seminal vesicle to record pressure. The tubes for monitoring blood pressure and intraluminal pressure of the seminal vesicle were connected to pressure transducer (Viggo-Spectramed P23XL-1). And the responses were recorded by a Gould RS 3400 polygraph. This study is divided into four parts:

Dose response curve of dopamine

Dopamine (10^{-6} to 10^{-4} mM/100g) was injected via the catheter from the femoral artery to the bifurcation of the common iliac artery for determining the dosage to achieve the maximal pressure response of the seminal vesicle. This dosage will be used in the following studies.

Spinal Cord Trans-section

To investigate the relationship between central and peripheral dopaminergic system on the rat seminal vesicle, cervical spinal cord trans-section was performed just before dopamine administration.

Pretreatment with sympatholytic agents

Guanethidine (10^{-6} to 10^{-5} mM/100g), phenoxybenzamine (10^{-7} to 10^{-6} mM/100g), prazosin (10^{-8} to 10^{-6} mM/100g), WB-4101 (10^{-8} to 10^{-6} mM/100g), chloroethylclonidine (10^{-8} to 10^{-6} mM/100g), yohimbine (10^{-8} mM/100g) and propranol (10^{-6} to 10^{-5} mM/100g) were injected via the catheter from the femoral artery to the bifurcation of the common iliac artery 20 minutes before the administration of dopamine to see the seminal vesicle pressure responses of each

drug.

Pretreatment with dopamine antagonists and atropine

Haloperidol (10^{-7} to 10^{-6} mM/100g), R(+)-SCH 23390 (10^{-8} to 10^{-6} mM/100g), domperidone (10^{-7} to 10^{-6} mM/100g), S(-) sulpiride (10^{-7} to 10^{-6} mM/100g) and atropine (10^{-8} mM/100g) were injected via the catheter from the femoral artery to the bifurcation of the common iliac artery 20 minutes before the administration of dopamine to see the seminal vesicle pressure responses of each drug.

Statistical Analysis

Phasic tension (á ñmmHg) of the maximal seminal vesicle contractile response induced by intra-arterial injection of dopamine was used as the control of this study. The seminal vesicle contractile responses after pretreatment with sympatholytic drugs, dopamine antagonists and atropine, and cervical spinal cord trans-section will be used to compare the control data. Student's *t*-test was used to assess unpaired comparison, with *PY* 0.05 indicating significance.

Results

The maximal pressure response of seminal vesicle was achieved by intra-arterial injection of 10^{-4} mM/100g dopamine and the mean phasic tension was 61.3 ± 4.1 mmHg. Systemic blood pressure increased simultaneously with intravesicle pressure response after dopamine injection. The rats were able to tolerate the whole procedure without evidence of pulmonary edema.

Pretreatment with sympatholytic agents suppressed the seminal vesicle pressure response significantly. The mean phasic tension of guanethidine (10^{-5} mM/100g), phenoxybenzamine (10^{-7} mM/100 g), prazosin (10^{-8} mM/100g), WB-4101 (10^{-8} mM/100g), chloroethylclonidine (10^{-7} mM/100 g) and yohimbine (10^{-8} mM/100g) were 33.3 ± 5.7, 43.8 ± 4.1, 46.5 ± 4.3, 43.2 ± 9.4, 37.2 ± 7.7 and 30.8 ± 6.7 mmHg respectively. This implied the involvement of noradrenergic nerve in this process. The action of dopamine was possibly mediated via α1 (especial α1A) and α2 adrenergic receptors. High dose of propranolol (10^{-6} mM/100g) could not suppress this contractile response. β adrenergic receptor was not excited in this pressure response.

Pretreatment with dopamine antagonists inhibited the pressure response of seminal vesicle to exogenous dopamine administration significantly also. The mean phasic tension of haloperidol ($5x10^{-6}$ mM/100g), R(+)-SCH 23390 (10^{-8} mM/100g), domperidone (10^{-7} mM/100g)and S(-) sulpiride ($5x10^{-7}$ mM/100g) were 28.8 ± 4.3, 22.8 ± 6.3, 43 ± 3.6 and 45.8 ± 7.8 mmHg respectively. This indicated the excitement of dopaminergic receptors (especial D1).

Pretreatment with atropine (10^{-8} mM/100g) and cervical spinal cord trans-section

inhibited the pressure response of seminal vesicle to dopamine significantly, and the mean phasic tension were 27.6 ± 4.8 and 37 ± 4.9 mmHg. The involvement of cholinergic nervous systems on the seminal vesicle pressure response to exogenous dopamine was possible. Cervical spinal cord trans-section decreased the pressure response induced by dopamine; this strongly suggested that CNS regulated the dopaminergic system of the rat seminal vesicle.

Discussion

Central dopaminergic system regulates the sexual behavior has well been demonstrated.[1-6] Dopaminergic receptors are able to be demonstrated on the smooth muscle cells and the glandular tissue of seminal vesicle by autoradiographic technique.[17] Dopamine and noradrenaline co-existed in the same sympathetic neurons[20] and the dopaminergic receptors located presynaptically were also proved.[14, 21-24] However, the neuroregulation between the central and the peripheral dopaminergic system is still unclear. Cervical spinal cord trans-section suppressed the seminal vesicle pressure response induced by exogenous dopamine administration indicated the involvement of downward neuroregulation from the CNS to the seminal vesicle. Higher dosage of guanethidine (10^{-5} mM/100g) is needed to suppress the seminal vesicle pressure response induced by exogenous dopamine implied the involvement of postganglionic sympathetic neuron.

Dopamine has mixed presynaptic actions (release endogenous noradrenaline) and postsynaptic actions. The postsynaptic actions of dopamine are likely to be mediated by alpha-adrenoceptors rather than by specific receptors[26, 27] prejunctional $\alpha 2$ [28] and postjunctional $\alpha 1$ adrenoceptors[29] may be involved. However, the real neuroregulation of dopamine is via dopaminergic or noradrenergic receptor is still unclear. Lower dosage of phenoxybenzamine (10^{-7} mM/100 g) suppressed the pressure response induced by exogenous dopamine significantly but not for propranolol (10^{-6} mM/100g) indicated the involvement of α adrenoceptor in this process. Pretreatment with prazosin (10^{-8} mM/100g), WB-4101 (10^{-8} mM/100g) and yohimbine (10^{-8} mM/100g) suppressed the pressure response significantly. Both of $\alpha 1$ (especial $\alpha 1A$) and $\alpha 2$ adrenoceptors were activated in the dopamine induced seminal vesicle contraction.

Haloperidol ($5x10^{-6}$ mM/100g) inhibited the seminal vesicle pressure response to dopamine implied the activation of dopamine receptor. Lower dosage of R(+)-SCH 23390 (10^{-8} mM/100g), compared to domperidone (10^{-7} mM/100g) and S(-) sulpiride ($5x10^{-7}$ mM/100g) suppressed the pressure response significantly. This indicated the dopaminergic receptors were excited, especial D1 receptor.

Small dosage of atropine (10^{-8} mM/100g) suppressing the pressure response induced by dopamine was amazing. Zarrindast MR et al showed that atropine

decreased the frequency of ejaculation, and concluded that D2 activation induces ejaculation through influence on cholinergic mechanisms.[30] The involvement of cholinergic nervous system was possible but need to do further investigation.

In conclusion, peripheral dopaminergic system existed in the rat seminal vesicle and regulated by CNS. The dopaminergic receptor was activated via noradrenergic nerve; properly via α2 (presynaptic) and α1A (postsynaptic) adrenoceptors in the dopamine induced seminal vesicle contraction. The cholinergic nervous system involved in this process was possible but need to do further investigation.

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