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Research Article

Region Dependent Differences in Cholinergic Responsiveness of Rabbit Vas Deferens: An *In Vivo* Animal Study

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Abstract

Introduction: Contractile responses on electric field stimulation of the rabbit vas deferens proximal and distal parts of vagus and pelvic nerve were compared. Parasympathetic nerves - vagus and pelvic - activation by electrical field stimulation caused different smooth muscles contraction in proximal and distal vas deferens parts.

Materials and Methods: The vas deferens Electromyogram (EMG) was measured by Nihon Kohden, Neurofax, EEG 4400, using surface bipolar silver electrodes (contact area 1.5-2.0 mm2, distance between electrodes 1.5 mm) for extracellular recordings of slow waves frequency and amplitude.

Results: Electric field stimulation of the vagus nerve markedly increased proximal part contraction of the right and left branches of the rabbit vas deferens. Electric field stimulation of the тазового нерва predominantly induce distal pats of the right and left branches of the rabbit vas deferens.

Conclusion: These findings may indicate that contribution of cholinergic to the contractile response of the proximal part of the rabbit vas deferens is different from that of the distal one.

Keywords: Cholinergic; Contractions; Smooth muscle; Vas deferens

Introduction

The vas deferens is a tiny paired muscular duct that transmits spermatozoa and seminal fluids from the epididymis and seminal vesicles to the ejaculatory duct. The vas deferens conditionally may be divided in three almost equal parts, proximal (epidydimal), medial, and distal (prostatic). Their physiological role in accumulation, maturation, nourishment, and transport may be different. There is evidence for an active role of the distal part of the vas in sperm maturation and nourishment [1].

Cholinergic system regulates vas deferens contractive activity of many kinds of animals (rats, guinea pigs, cats, and rabbits). Parasympathetic ganglion electrical stimulation lead to spermatic, ejaculation ducts and spermatic vesicles contractility. The presence of cholinergic nervous elements in the vas deferens mostly localized in the circumferential muscles layer is confirmed immunohistochemically. Cholinergic nerves originate from the pelvic plexus where the sympathetic and parasympathetic ganglia are located. Cholinergic nerves account for main volume of the genitourinary tract vegetative innervation [2]. Presynaptic nicotinic receptors activation is promotive of acetylcholine release in the aganglionic vas deferens [3,4], nerve filaments of which are susceptible to tetrodotoxin but not to bretilium. Cyclopentane, a

M-cholinergic receptor antagonist, caused these nerves contractility, which was turned off by neostigmine, an acetylcholinesterase inhibitor. The contractility was intensified by nicotine (30 μM), which is indicative of the presence of presynaptic n-receptors on fibers affecting acetylcholine release [5]. These data imply the presence of N-cholinoreceptors and M- cholinoreceptors, cholinergic excitement transmission components, in a vas deferens.

Ca^{2+} visualization demonstrated that nicotine and its agonists stimulate mouse vas deferens nervous terminals [6]. At the same time, bretylium, an adrenergic sympatholytic, proved to be incapable to inhibit potential induced Ca^{2+} transient current in many nerve filament terminals [7]. In other words, cholinergenic agonists induce potentially induce Ca^{2+} transient current whereas the sympathetic terminals catecholamine release inhibitor (bretylium or ornid) doesn't have any effect on this process. There are 2 types of muscarinic receptors discovered in a vas deferens of rodents. They are presynaptic M_1 [8] and postsynaptic M_3-receptors, with the second taking part in intensification of neurogenic contractions [5]. In other words, the vas deferens of rodents is innervated with cholinergic nerves, the function of which is limited by cholinesterase and is regulated by activated muscarinic receptors. However, the role of cholinergic system in vas deferens regulation is underestimated.

Materials and Methods

The experiments were performed under Nembutal general anaesthesia (40 mg/kg in min) on 24 chinchilla rabbits weighing 3.5-4 kg. Electromyogram (EMG) of proximal and distal parts of the right and left vas deferens were registered with bipolar silver electrodes with contact area of 1.5-2 mm^2 and anode-to-cathode distance of 1.5 mm. Nerve innervation was performed with the help of nerve impulses with the length of 2 ms, amplitude 1.5-15 mV and frequency 10 Hz. The EMG amplitude (mV) and frequency of slow waves were registered. The experiments were performed with registration of vas deferens EMG as a response to electrical innervation (hereinafter - simply "innervation") of peripheral division of the right nervus vagus on the neck and a peripheral division of the pelvic nerve. The optimal conditions ("optimum") of innervation were identified, at which the scope of EMG stimulation wasn't by more than twice background EMG and there was no slow waves frequency rise following long-term innervation of the nervus vagus and the pelvic nerve. Parasympathetic (including the pelvic nerve) influence on the contractile activity of proximal and distal divisions of vas deferens were studied.

Results

Proximal Division of The Right Vas Deferens

Stimulation of peripheral division of the right nervus vagus resulted in activation of electromotor activity slow waves of the right vas deferens proximal division from 14.0±1.7 to 18.0±1.3 / min (28.5%, $p<0.05$), amplitude from 0.17±0.03 to 0.25±0.03 mV (47%, $p<0.05$).

5.1.1 Pelvic Nerve Stimulation: Stimulation of the right pelvic nerve peripheral division leads to activation of the electromotor acivity slow waves of the right vas deferens by 30% ($p<0.05$), amplitude - by 31% ($p<0.05$).

(Table 1) Electromotor activity of the right vas deferens proximal division under stimulation of the parasympathetic nerve (frequency, in min; amplitude, mV)

Parasympathetic nerve	Background		Parasympathetic nerve stimulation	
	frequency	amplitude	frequency	amplitude
Nervus vagus	14.0±1.7	0.17±0.03	18.0±1.3*	0.25±0.03*
			28.5%	47%
Pelvic nerve	11.3±1.2	0.19±0.03	14.7±1.3*	0.25±0.03*
			30%	31%
*p<0.05				

Table 1: Demonstrates that it's the bulbar part of the parasympathetic nervous system that takes the main part in regulation of contractile activity of the proximal division of the right vas deferens.

Right Vas Deferens Distal Division

Nervus Vagus Stimulation: Stimulation of the right nervus vagus peripheral division leads to activation of the slow waves of electromotor activity of the vas deferens; EMG slow waves frequency increases from 9.8±0.8 to 13.3±1.2 /min (35.7%; $p<0.05$), with stable amplitude (0.23±0.03 mV).

Pelvic Nerve Stimulation: Stimulation of the right pelvic nerve peripheral division leads to activation of slow waves of EMG of the vas deferens; EMG slow waves frequency increases by 30.7% ($p<0.05$), and amplitude by 31.6% ($p<0.05$) (Table 2). EMG activity of the right vas deferens distal division under stimulation of the parasympathetic nerve (frequency, in min; amplitude, mV)

Parasympathetic nerve	Background		Parasympathetic nerve stimulation EMG	
	frequency	amplitude	frequency	amplitude
Nervus vagus	9.8±0.8	0.23±0.03	13.3±1.2*	0.23±0.03
			35.7%	0%
Pelvic nerve	11.3±1.2	0.19±0.03	14.7±1.3*	0.25±0.03*
			30.1%	31.6%
*p<0.05				

Table 2: Demonstrated that the right vas deferens distal division is stimulated mainly by pelvic nerve.

Left Vas Deferens Proximal Division

Nervus Vagus Stimulation: Stimulation peripheral division of the nervus vagus leads to activation of slow waves of electromotor activity of the left vas deferens proximal division; EMG slow waves frequency increases from 9.8±0.5 to 12.7±0.7 /min (29.6%, p<0.05), and amplitude from 0.21±0.03 to 0.26±0.05 mV (23.8%, p,0.05).

Pelvic Nerve Stimulation: Stimulation of the pelvic nerve peripheral division leads to activation of slow waves of electromotor activity of the left vas deferens proximal division; EMG slow waves frequency increases by 37.9% (p<0.05), and amplitude by 47.1% (p<0.05) (Table 3). In other words, the pelvic nerve stimulatory effect is higher than that of the nervus vagus.

(Table 3) EMG activity of the left vas deferens proximal division under stimulation of the parasympathetic nerve (frequency, in min; amplitude, mV)

Parasympathetic nerve	Background		Parasympathetic nerve stimulation	
	frequency	amplitude	frequency	amplitude
Nervus vagus	9.0±0.5	0.21±0.03	12.7±0.7*	0.26±0.05*
			41.3%	23.8%
Pelvic nerve	8.7±0.3	0.17±0.02	12.0±0.8*	0.19±0.05*
			37.9%	11.8%
*p<0.05				

Table 3: Shows that the left vas deferens proximal division is stimulated mainly by the nervus vagus.

Experimental Studies of The Left Vas Deferens Distal Division

Nervus vagus stimulation: Stimulation of the nervus vagus peripheral division leads to activation of slow waves of electromotor activity of the left vas deferens proximal division: the EMG slow waves frequency increased from 9.5±0.5 to 15.5±1.3 /min (63.2%; p<0.05), and amplitude from 0.15±0.03 to 0.16±0.04 mV (6.7%; p<0.05).

Pelvic nerve stimulation: Stimulation of the pelvic nerve peripheral division division innervations leads to slow waves of electromagnetic activity of left vas deferens proximal division leads to activation of slow waves of the electromotor activity of the left vas deferens distal division; EMG slow waves frequency increases by 50% (p<0.05), and amplitude by 233.3% (p<0.001) (Table 4). EMG activity of the left vas deferens distal division under stimulation of the parasympathetic nerve (frequency, in min; amplitude, mV).

Parasympathetic nerve	Background		Parasympathetic nerve innervation	
	frequency	amplitude	frequency	amplitude
Nervus vagus	9,0±0,5	0,15±0,03	15,5±1,3*	0,16±0,04
			63,2%	6,7%
Pelvic nerve	9,0±0,5	0,15±0,03	13,5±0,9*	0,5±0,05*
			50,0%	233,3%
*p<0.05				

Table 4: Demonstrates that left vas deferens distal division is stimulated mainly by the pelvic nerve.

The pelvic nerve is of the main importance in the parasympathetic regulation of the left vas deferens distal division electric and motor activity, the effect of which is dramatically higher than that of the nervus vagus.

Conclusions

This study is a stage of studies of regulation of the motor function of the smooth muscle organs of the female and male genital sphere by the cholinergic and serotonergic parts of the autonomic nervous system [9]. The experiments on different sections of the right and left vas deferens demonstrate that stimulation of the peripheral segment of the parasympathetic nerve causes an increase of the electromotor activity of the vas deferens. This study was aimed to evaluate the regional distribution of cholinergic influence on vas deferens. Distal sections of the left and right vas deferens are proved to be stimulated primarily by the pelvic nerve. Proximal sections of the left and right vas deferens are stimulated primarily by the vagus nerve.

It has been shown that the cholinergic effect on the motor function of the right vas deferens dominates over the motor activity of the left vas deferens, which reflects the general tendency of predominance of the cholinergic effect on the motility of each right-side lateralization from a pair of organs of the genitourinary sphere (the right vas deferens, the right ureter, the right uterine tube). These studies may have clinical implication because they confirm highly stable biological control of the vas deferens motility. what can make a difference in male fertility.

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