COMPARISON OF EFFECTS OF CENTRAL CHOLINOLYTICS OF MUSCARINIC AND NICOTINIC ACTION ON MOTOR FOOD CONDITIONED REFLEXES AND SEXUAL BEHAVIOR OF MALE RATS

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The central muscarinic cholinolytic drug benactyzine (2, 8, 15 mg/kg) weakened both excitatory and inhibitory processes. Central nicotinic cholinolytic drugs pediphen and IÉM-506, in the same doses, improved the rats' conditioned-reflex activity. Large doses of these drugs (30 and 50 mg/kg) had an inhibitory action on conditioned-reflex activity. Disturbances of the sexual behavior of male rats appeared after small doses of benactyzine (in a dose of 1 mg/kg it reduced the frequency of copulation, while in a dose of 15 mg/kg it caused complete cessation of sexual activity). Pediphen and IÉM-506, given in doses inhibiting conditioned-reflex activity, caused no changes in the sexual behavior of the rats.

EXPERIMENTAL METHOD

Over a period of 2 months, motor food conditioned reflexes were developed in a maze in 15 male rats weighing 180-230 g and stabilized [5]. Experiments to study the effect of central cholinolytics on sexual behavior were carried out on 20 male rats weighing 200-250 g. Animals copulating actively with receptive females were chosen by preliminary tests lasting 90 min. The female rats received an injection of 0.1 ml 0.1% oily solution of diethylstilbestrol propionate 2 days before the experiment. The experiments were carried out in a soundproof room during the evening.

The central muscarinic (M–) cholinolytic benactyzine (2-diethylaminoethyl benzilate hydrochloride) [2,4], and the nicotinic (N-) cholinolytic pediphen (1,1-diphenyl-5-diethylaminopentane hydrochloride) [3,8] were injected subcutaneously 30 min before the experiment. In the experiments to study conditioned reflexes the rats were used once every 5 days, and in those to study sexual behavior, once every 7 days.

The experimental results were subjected to statistical analysis [1]. Effective doses of the central cholinolytics were compared by their action on the motor food conditioned reflexes and on the sexual behavior of male rats.

EXPERIMENTAL RESULTS AND DISCUSSION

Benactyzine in doses of 0.5 and 1 mg/kg reduced the latent period of the conditioned-reflex response (Table 1). An increase in the dose of benactyzine to 20 mg/kg and above increased both the latent period of the reflex and the time taken by the animal to reach the feeding bowl; the number of inter-trial responses was increased and differentiation disturbed. Benactyzine in a dose of 30 mg/kg caused marked disturbances of conditioned-reflex activity (the animal did not run to the feeding bowl on application of the positive conditioned stimulus, differentiation was disturbed, intertrial responses were frequent).

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TABLE 1. Comparison of Effects of Central M - and N- Cholinolytics on Conditioned-Reflex Activity of Male Rats

Drug	Dose (in mg /kg)	Conditioned-reflex activity			
		latent period (in sec)	time to run through maze (in sec)	disturbance of differentiation (in percent)	total number of intertrial responses
Physiological saline		1,93±0,05	4,12±0,10	4,1	13
Benactyzine	0,5	1,73±0,10	4,03±0,11	4,1	14
	1	1,84±0,06	4,10±0,08	—	13
	2	2,12±0,05[1]	4,37±0,09	8,2	23
	4	2,26±0,07[1]	4,57±0,10[1]	8,2	28
	8	2,61±0,09[1]	4,72±0,09[1]	16,3	23
	15	3,12±0,13[1]	5,31±0,13[1]	25	25
	20	3,35±0,14	5,62±0,13[1]	70,8	39
	30	Severe disturbances of conditioned-reflex activity			
Pediphen	2	1,81±0,03	4,08±0,08	4,1	9
	4	1,57±0,06[1]	3,82±0,06[1]	4,1	13
	8	1,34±0,07[1]	3,72±0,06[1]	—	5
	15	1,71±0,10	4,07±0,11	4,1	7
	20	2,11±0,09	4,31±0,08	—	7
	30	Complete cessation of conditioned-reflex activity			
Physiological saline		2,15±0,05	3,54±0,15	—	5
IÉM-506	2	1,69±0,08[1]	3,31±0,15	5,4	3
	8	1,60±0,07[1]	3,30±0,08	—	3
	20	2,44±0,12	4,00±0,23	—	—
	40	Complete cessation of conditioned-reflex activity			

TABLE 2. Comparison of Effects of Central M- and N- Cholinolytics on Sexual Behavior of Male Rats

Drug	Dose (in mg/kg)	Sexual behavior		
		latent period (in sec)	no. of cop., intromissions in 90 min	tol. dur. of refract. per. (in min)
Physiological saline		40—80	76,1±3,6	42,5±2,5
Benactyzine	0,5	40—80	74,1±3,2	42,5±2,5
	1	40—80	52,3±3,5[1]	51,4±3,2
	2	40—80	51,5±3,6[1]	56,3±2,6[1]
	4	40—80	35,7±3,6[1]	61,7±4,2[1]
	8	40—80	29,2±2,7[1]	72,7±2,6[1]
	15	Cessation of sexual activity		
Physiological saline		40—80	64,5±3,8	50,7±3,8
Pediphen	8	40—80	66,7±2,4	55,0±3,1
	20	40—80	65,5±4,2	53,1±3,5
	30	40—80	57,9±4,8	49,6±1,9
	50	6,7±1,6 min	56,1±3,6	47,1±2,6
Physiological saline		40—80	53,7±2,7	60,2±3,1
IÉM-506	8	40—80	51,7±2,9	57,5±3,1
	20	40—80	52,9±2,7	56,5±3,3
	40	40—80	58,3±2,7	57,7±2,7
	80	40—80	28,9±2,2[1]	71,7±2,8[1]
Oxyphenonium bromide	20	40—80	53,8±2,7	54,3±2,1
	40	40—80	48,7±2,6	58,9±2,3

Injections of the central N- cholinolytic drug pediphen (4 and 8 mg/kg) caused a significant shortening of the latent period and of the time taken by the animal to reach the feeding bowl. With an increase in the dose of the drug to 20 mg/kg the latent period and the time taken to run through the maze were increased.

Differentiation was not disturbed. In some cases the animal did not run to the feeding bowl in response to a positive conditional stimulus. Administration of pediphen in a dose of 30 mg/kg was accompanied by total inhibition of conditioned-reflex activity.

In the experiments to study the effects of the central M- and N- cholinolytics on sexual behavior of the male rats it was found that benactyzine in a dose as low as 1 mg/kg caused a significant decrease in sexual activity of the animals (an increase in the total duration of the refractory periods, a decrease in the number of copulations with intromissions), while in a dose of 15 mg/kg it caused the complete cessation of sexual activity (Table 2). Under the influence of the central N- cholinolytic pediphen, changes in sexual behavior of the male rats were observed only if the drug was given in a dose of 50 mg/kg (increase in latent period).

Another central N- cholinolytic was used in the experiment. This was IÉM-506, which differs from pediphen in its chemical structure (1-ethyl-2-diethylaminoethyl diphenylacetate hydrochloride) [6]. Its effect on conditioned-reflex activity was studied in 6 male rats and on sexual behavior in 10 male rats. In doses of 2 and 8 mg/kg compound IÉM-506 improved conditioned-reflex activity of the male rats (Table 1). When given in a dose of 20 mg/kg it reduced conditioned-reflex activity, and as the dose was increased up to 400 mg/kg suppressed it completely. Changes in the sexual behavior of the male rats (a decrease in the number of copulations) was observed only when the compound was given in a dose of 80 mg/kg.

The results of these experiments thus demonstrate marked differences in the action of central M- and N-cholinolytics on conditioned-reflex activity and sexual behavior of male rats. Whereas the effect of the central M- cholinolytic benactyzine, given in average doses, was expressed as weakening of excitatory and inhibitory processes (an increase in the length of the latent period and in the time taken to run to the feeding bowl, de-inhibition of differentiation), under the influence of the central N-cholinolytics pediphen and IÉM-506, given in the same doses, the predominant effect was strengthening of excitation without any disturbance of inhibition. Large doses of benactyzine, pediphen, and compound IÉM-506 inhibited conditioned-reflex activity. It is important to note that changes in the sexual behavior of the male rats were observed after administration of benactyzine in doses much smaller than those required to disturb conditioned-reflex activity. By contrast, changes in conditioned-reflex activity of the male rats produced by central N-cholinolytics pediphen and compound IÉM-506 appeared much sooner than disturbances of the animals' sexual behavior. It can be assumed that the predominant role in the inhibition of the sexual behavior of the male rats was played by central M-cholinergic systems. This conclusion is confirmed by the results of the experiments with oxyphenonium bromide, a drug with a marked peripheral M- cholinolytic action [7, 9]. Its administration in doses of 20 and 40 mg/kg caused no changes in the sexual behavior of the male rats.

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