ACTION OF NEUROTRANSMITTERS ON ACTIVITY OF THE SURFACTANT SYSTEM AND FUNCTIONING AREA OF THE LUNG

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Experimental research and clinical observations have demonstrated the effect of neurotransmitters on respiratory and circulatory function [2, 5]. Considerable attention during the study of the system responsible for gas exchange has been devoted in recent years to the surfactant system of the lungs [10]. However, mediator regulation of the lungs has not been adequately studied, and the investigation described below was carried out to fill this gap.

EXPERIMENTAL METHOD

Experiments were carried out on albino rats weighing 200-300 g. The animals as a whole were divided into three groups. In group 1 the role of functional activity of the sympathicoadrenal system in changes in surfactant activity and the functioning area of the lung (FAL) was investigated in 42 animals (three series of experiments, 14 animals in each series). In group 2 the state of the surfactant system and FAL depending on activity of the cholinergic system was studied in 48 animals (four series of experiments, 12 rats in each series). In group 2 activity of the serotoninergic system of the blood, the surface-active complex of the lung, and FAL was studied in 50 animals (five series, 10 animals in each series).

Catecholamine saturation was produced by subcutaneous injection of a combination of adrenalin and noradrenalin, 100 μg/kg of each twice a day for 7 days. A deficiency of biogenic amines was created by means of the α-adrenoblocker droperidol in a dose of 0.1 mg/kg and the β-adrenoblocker propranolol (obsidan) in a dose of 1 mg/kg, for 7 days, or by extirpation of the chromaffin tissue of the adrenals by total removal of the right adrenal and destruction of the medulla of the left adrenal with a thermocautery [3].

In the next series of experiments adrenalin and noradrenalin in doses of 100 mg/kg were injected into animals with catecholamine deficiency and activity of the surfactant system of their lungs and FAL were determined. An artificial excess of the cholinergic mediator was created by intraperitoneal injection of acetylcholine in a dose of 100 μg/kg for 7 days. A deficiency of acetylcholine was created by partial depancreatization. In two series of experiments on depancreatized rats, to correct disturbances in cholinergic systems after the operation and until the day of the experiments, acetylcholine (100 μg/kg) or lipocaine (50 units daily) was injected.

An excess of serotonin in the body was created by intraperitoneal injection of serotonin (100 μg/kg) or tryptophan (100 μg/kg) for 10 days.

A deficiency of the serotoninergic complex was induced by partial depancreatization and also by a pharmacologic method ("poisoning" with reserpine). The catecholamine deficiency thus arising was compensated by injection of adrenalin and noradrenalin in a dose of 100 mg/kg before the experiment.

Activity of the surfactant system of the lung was studied by a stalagmometric method [9]. FAL was estimated morphometrically [11].

The total catecholamine level in the peripheral blood was determined by Shaw's method in Matlina's modification [6, 7], the acetylcholine concentration was determined by biological [12] and chemical methods [9], ac-

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TABLE 1. Level of Activity of Adrenergic, Cholinergic, Serotoninergic, and Surfactant Systems and FAL in Rats with an Artificial Excess of One Mediator (M ± m)

Parameter	Type of experiment	Control	Experiment
ACh	Injection of acetylcholine	27,70±0,72	11,64±6,41
AChE		85,90±1,11	68,50±0,36
BChE		48,20±0,87	119,20±1,26
ST		61,90±0,17	59,40±0,41
FAL		94,31±2,03	99,70±0,47
ACh	Injection of lipocaine	26,02±0,62	33,56±0,67
AChE		89,99±1,96	91,38±1,12
BChE		48,62±1,73	59,59±0,51
ST		62,30±0,18	59,70±1,09
FAL		92,42±1,12	98,70±0,57
CCh	Injection of adrenalin and noradrenalin	40,00±0,57	78,00±0,73
ST		62,50±0,21	60,00±0,57
FAL		93,10±0,27*	94,30±1,53
5-HT	Injection of tryptophan	5,11±0,19	11,36±0,23
MAO		0,02±0,00	0,04±0,00
ST		62,10±0,15	58,70±0,18
FAL		92,90±2,34*	95,70±0,48
5-HT	Injection of serotonin	4,54±0,21	6,81±0,25
MAO		0,03±0,00	0,03±0,00
ST		62,70±0,62	59,40±0,41
FAL		95,30±1,34	98,70±0,54

Legend. Here and in Table 2: CCh) total catecholamines (in relative units/ml), ACh) acetylcholine (in nanomoles/liter), BChE, AChE) butyl- and acetylcholinesterase activity respectively (in nanomoles/h/liter), 5-HT) serotonin (in nanomoles/liter), MAO) (in nanomoles/h/liter), ST) surface tension, inversely proportional to surfactant concentration (in N/m), FAL (in %); *$P < 0.05$ compared with control.

TABLE 2. Parameters of Adrenergic, Cholinergic, Serotoninergic, and Surfactant Systems and Functional Area of the Lung in Rats with an Artificial Deficiency of One Mediator (M ± m)

Parameter	Type of experiment	Control	Experiment
ACh	Depancreatization	26,59±0,80	4,11±0,33
AChE		41,78±0,94	20,55±0,82
BChE		82,88±0,12	39,73±1,64
ST		62,81±0,58	67,20±1,32
FAL		93,82±1,47	72,10±0,57
CCh	Demedullation	39,00±0,89	1,13±0,24
ST		61,90±1,13	65,90±0,87
FAL		91,90±0,51	84,20±1,23
CCh	Injection of droperidol and propranolol	38,10±0,92	1,21±0,11
ST		63,20±1,07*	64,70±0,29
FAL		92,60±1,03	87,90±0,37
5-HT	Injection of reserpine	5,65±0,18	0,28±0,26
MAO		0,21±0,00	0,0056±0,0003
ST		60,90±0,21	69,20±0,37
FAL		95,10±0,10	79,70±1,25
5-HT	Depancreatization	5,11±0,36	0,40±0,03
MAO		0,0280±0,0007	0,014±0,001
ST		61,50±1,25	71,40±1,05
FAL		94,37±1,25	81,90±1,21

tivity of acetyl- and butylcholinesterases by the method in [13], the serotinin level by a biological method [11], and monoamine oxidase (MAO) activity by Soloimskaya's method, based on loss of serotonin [8]. The significance of differences was determined by Student's test.

EXPERIMENTAL RESULTS

It will be clear from Table 1 that injection of adrenalin and noradrenalin increased the total blood monoamine concentration and was accompanied by a decrease in surface tension (inversely proportional to the sur-

factant concentration) and an increase in FAL. After demedullation the catecholamine content fell and this was accompanied by a fall in activity of the surfactant system and FAL. Similar results were obtained after α- and β-adrenoreceptor blockade by droperidol and propranolol (Table 2).

Creation of an excess of cholinergic mediator by injecting acetylcholine into intact animals, and also by injecting lipocaine, which participates in acetylcholine synthesis, caused an increase in reactivity of the cholinergic systems of the blood, surfactant, and FAL (Table 1).

Experimental reproduction of acetylcholine deficiency by depancreatization reduced the mediator concentration and cholinesterase activity on the 7th-8th day. The surfactant was exhausted and, at the same time, FAL decreased.

Preliminary injection of serotonin or tryptophan for 7 days increased activity of the serotoninergic and surfactant systems, and FAL also was increased (Table 1).

A serotonin deficiency caused by partial depancreatization led to a decrease in activity of the serotoninergic system, of surfactant activity, and of FAL.

In the animals receiving reserpine, which inhibits biological activity of serotonin, the serotonin concentration and MAO activity in the peripheral blood fell, and this was accompanied by exhaustion of surfactant and a decrease in FAL (Table 2).

After injection of acetylcholine into animals with an experimentally induced deficiency of the mediator the state of the surfactant system and FAL were within normal limits. Parameters of the adrenergic, cholinergic, and serotoninergic systems showed no significant change.

The results are evidence that acetylcholine, catecholamines, and serotonin influence the surfactant system of the lungs, and ultimately this is reflected in FAL. Each mediator has its own type of action. This is evidently associated with the trophic action of neurotransmitters [4, 14].

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