EFFECT OF LITHIUM ON THE CATECHOLAMINE CONCENTRATION IN THE RABBIT AND RAT BRAIN

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A single injection (200 mg/kg, intraperitoneally) or a course of injections (100 mg/kg subcutaneously, daily for 10 days) of lithium chloride given to rats had no significant effect on the content of catecholamines and dihydroxyphenylalanine in the brain stem 1 and 4 h after the injections. In experiments on rabbits the compound (100 mg/kg, intravenously) increased the noradrenalin concentration in the thalamus, hypothalamus, reticular formation, and caudate nucleus. An increase in the dopamine content in the caudate nucleus was accompanied by a simultaneous decrease in its concentration in the thalamus, hypothalamus, reticular formation, amygdala, and hippocampus.

KEY WORDS: lithium chloride; catecholamines; brain.

With the obtaining of evidence of a possible role of central monoamines in the mechanism of the psychotropic action of lithium [4, 9-12, 14-16] and its uneven distribution in the various parts of the brain [6, 7] it was decided to study the effect of lithium chloride on the catecholamine and dihydroxyphenylalanine (DOPA) in the brain structures of rats and rabbits.

EXPERIMENTAL METHOD

Experiments were carried out on 84 male rats weighing 160-240 g and on 44 rabbits of both sexes weighing 2-2.5 kg. The rats received lithium chloride by single intraperitoneal injection of 200 mg/kg or by a course of subcutaneous injections of 100 mg/kg daily for 10 days; rabbits received a single injection of 100 mg/kg of a 10% solution of lithium chloride into the marginal vein of the ear. The animals were decapitated 1 and 4 h after injection of the preparation. The control animals received the corresponding volume of physiological saline.

TABLE 1. Effect of Lithium Chloride on Catecholamine and DOPA Content (in μg/g) in Brain Stem of Rats (M ± m)

Dose of compound (mg/kg)	Time after injection of compound, h	Adrenalin	Noradrenalin	Dopamine	DOPA
Control (n = 22)	—	0,05+0,002	0,63+0,023	6,40±0,171	0,05+0,003
200 (n = 14)	1	0,04+0,004	0,63+0,034	5,94+0,244	0,06+0,005
P		0,3	1	0,1	0,4
200 (n = 10)	4	0,05+0,006	0,59+0,054	6,20+0,238	0,05+0,006
P		1	0,4	0,5	1
Control (n = 20)	—	0,06+0,003	0,60+0,025	6,39+0,184	0,05+0,002
100 (n = 18) (daily for 10 days)	12	0,05±0,002	0,56±0,015	6,26±0,180	0,04±0,02
P		0,3	0,2	0,6	0,2

Note. Number of experiments shown in parentheses.

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TABLE 2. Effect of Lithium Chloride (100 mg/kg, intravenously) on Catecholamine and DOPA Content (in μg/g) in Brain Structures of Rabbits

Region of brain	Adrenalin			Noradrenalin			Dopamine			DOPA		
	Control	1 h	4 h	Control	1 h	4 h	Control	1 h	4 h	Control	1 h	4 h
Hypothal. + pituit.	0,14 ± 0,019	0,13 ± 0,015 0,7	0,14 ± 0,014 1	0,96 ± 0,148	1,13 ± 0,123 0,4	1,47 ± 0,116 0,01	16,8 ± 0,31	12,6 ± 0,87 0,001	15,1 ± 1,24 0,2	0,10 ± 0,007	0,11 ± 0,010 0,4	0,10 ± 0,007 1
p												
Thalamic region	0,06 ± 0,003	0,05 ± 0,008 0,2	0,06 ± 0,008 1	0,13 ± 0,010	0,22 ± 0,029 0,01	0,20 ± 0,020 0,01	3,9 ± 0,33	3,0 ± 0,14 0,03	2,9 ± 0,20 0,02	0,06 ± 0,010	0,05 ± 0,004 0,3	0,06 ± 0,005 1
p												
Reticular formation	0,05 ± 0,003	0,05 ± 0,007 1	0,05 ± 0,004 1	0,21 ± 0,028	0,18 ± 0,024 0,4	0,32 ± 0,040 0,05	4,9 ± 0,24	4,0 ± 0,40 0,07	4,2 ± 0,34 0,1	0,05 ± 0,004	0,06 ± 0,010 0,3	0,05 ± 0,002 1
p												
Caudate nucleus	0,10 ± 0,007	0,10 ± 0,010 1	0,12 ± 0,014 0,2	0,35 ± 0,045	0,52 ± 0,036 0,01	0,37 ± 0,053 0,76	4,8 ± 0,23	8,4 ± 1,05 0,005	7,2 ± 1,02 0,04	0,10 ± 0,016	0,08 ± 0,132 0,8	0,10 ± 0,007 1
p												
Hippocampus	0,06 ± 0,005	0,06 ± 0,005 1	0,07 ± 0,008 0,3	0,28 ± 0,030	0,22 ± 0,019 0,1	0,36 ± 0,043 0,15	4,5 ± 0,10	3,8 ± 0,26 0,03	4,1 ± 0,24 0,15	0,06 ± 0,004	0,06 ± 0,007 1	0,05 ± 0,004 0,09
p												
Amygdala	0,03 ± 0,009	0,08 ± 0,009 1	0,07 ± 0,008 0,4	0,20 ± 0,023	0,23 ± 0,033 0,5	0,22 ± 0,017 0,5	5,8 ± 0,36	4,3 ± 0,22 0,003	4,2 ± 0,18 0,001	0,03 ± 0,012	0,07 ± 0,009 0,6	0,06 ± 0,004 0,2
p												
Motor cortex	0,06 ± 0,004	0,06 ± 0,008 1	0,05 ± 0,007 0,1	0,16 ± 0,026	0,19 ± 0,019 0,4	0,21 ± 0,020 0,1	3,8 ± 0,24	3,2 ± 0,36 0,2	3,5 ± 0,40 0,56	0,06 ± 0,009	0,05 ± 0,005 0,3	0,06 ± 0,005 1
p												

Note. Number of experiments shown in parentheses.

Weighed samples of the various part of the brain (200-600 mg) were quickly frozen. Catecholamines and DOPA were determined by a spectrofluorometric method [5]. The brain structures studied are shown in Tables 1 and 2.

EXPERIMENTAL RESULTS AND DISCUSSION

In agreement with data in the literature [4, 8-10] lithium chloride, given by a single injection or a course of injections to rats, did not significantly change the catecholamine and DOPA content in the brain stem (Table 1).

Different results were obtained in the experiments on rabbits (Table 2). Injection of lithium chloride into the animals was accompanied by an increase in the noradrenalin concentration in most of the brain structures investigated. The clearest changes were found in the thalamus, where a marked increase in the noradrenalin concentration was observed 1 and 4 h after injection of the compound. The effect was rather less marked in the hypothalamus, reticular formation, and caudate nucleus. No significant change occurred in the noradrenalin level in the hippocampus, amygdala, and cortex.

The increase in the noradrenalin concentration discovered in certain structures of the rabbit brain, from the standpoint of the catecholamine hypothesis of the pathogenesis of affective disorders, could point to the participation of this amine in the mechanism of the antidepressive action of lithium salts.

Lithium chloride causes a redistribution of dopamine in the rabbit brain. The dopamine concentration was reduced by 16-28% in the thalamus, hypothalamus, reticular formation, and amygdala, whereas in the caudate nucleus the level of this amine rose sharply (by 75% after 1 h and by 50% after 4 h). In an additional series of experiments in which 300 mg/kg lithium chloride was injected intravenously into rabbits, the same pattern was observed: the dopamine concentration in the caudate nucleus was increased by 94 and 117% relative to the control after 1 and 4 h respectively.

The caudate nucleus is known to participate in the mechanism of broad inhibitory control over motor behavioral responses in higher animals and man. Considerable importance is attached to it in the development of manic-depressive psychoses [3]. It is also known that a basic mediator role in the nigro-striatal pathways is played by dopamine [1, 2], which inhibits the activity of most neurons of the corpus striatum. It is through dopamine that the nigro-striatal system exerts restraining control over the work of the neostriatum. It has been claimed that endogenous depression in man may be the result of blockade of dopamine receptors or exhaustion of dopamine in the presynaptic endings of the nigro-striatal pathways.

On the basis of these concepts, dopamine can be considered to play a part in the mechanism of the antidepressive properties of lithium. By increasing the dopamine concentration in neurons of the caudate nucleus, lithium in a depressive state abolishes the excessive inhibitory effect of this amine on other cerebral structures and, in particular, on the cortex.

No correlation has been found between the effect of lithium chloride on the catecholamine content and the accumulation of lithium in these same parts of the rabbit brain described previously [6, 7].

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