CATECHOLAMINE METABOLISM IN THE TISSUES OF GUINEA PIGS AFTER HEAD INJURY

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Experiments on guinea pigs showed that head injury produces initial activation (during the first 15 min after trauma) followed by inhibition of activity of the adrenal medulla. The adrenalin level fell in the hypothalamus and other parts of the brain 45 and 100 min after trauma, while the normetanephrine concentration rose. It is suggested that the decrease in the noradrenalin content discovered in the brain does not reflect inhibition of its synthesis, but increased inactivation of noradrenalin by O-methylation, which leads to an increase in the normetanephrine content.

After closed head injuries activation of the sympathico – adrenal system and of the hypothalamo – hypophyseo – adrenocortical system is observed [2, 3, 6, 8, 12]. Similar responses have been described in other states of stress.

Catecholamine metabolism in various forms of stress has been investigated on many occasions [1, 4, 7, 11, 14, 15, 19, 21]. A feature distinguishing the stress response after head injury is a lesion of the hypothalamus and brain stem [2], the region responsible for adaptive reactions.

The object of the present investigation was to study the content of catecholamines, DOPA, and normetanephrine in the brain and, in particular, the hypothalamus, and in the adrenals and blood of guinea pigs at various times after head injury.

EXPERIMENTAL METHOD AND RESULTS

Experiments were carried out on male guinea pigs weighing 320-370 g. The tissue levels of adrenalin, noradrenalin, and DOPA [11], dopamine [10], and normetanephrine [9] were investigated. Head injury was inflicted by a measured blow from a metal rod on the head.

During the first 15 min after head injury the catecholamine content in the adrenals was unchanged (Table 1), while the content of their precursors was increased (dopamine by 18%, DOPA by 30%). Meanwhile the blood adrenalin concentration was increased by 45%. The increased liberation of adrenalin into the blood stream was thus balanced by its increased formation. This accounts for the apparent stability of the adrenalin concentration in the adrenals. Later (after 45 and 100 min, and 12 h) the content of adrenalin and its precursors in the adrenals fell by 35-40%. However, the adrenalin concentration in the blood fell appreciably (by 40%) only when 12 h had elapsed after injury. It thus follows that the increase in the blood adrenalin concentration in the first 100 min and its subsequent decrease 12 h after injury can be regarded as the result of initial activation and subsequent inhibition of activity of the adrenal medulla.

The work of Kassil' et al. [5, 6] has shown that the permeability of the blood-brain barrier is increased after head injury, and this may explain the vary considerable (200%) increase in the adrenal level in the hypothalamus 100 min after trauma.

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TABLE 1. Content of Catecholamines, DOPA, and Normetanephrine in the Tissues (in μg/g) and Blood (in μg/liter plasma) in Guinea Pigs at Different Times after Head Injury (M±m)

Time elapsing after injury	n	adrenals: Adrenalin	adrenals: Noradrenalin	adrenals: Dopamine	DOPA	Normetanephrine	blood: Adrenalin	blood: Noradrenalin
Normal	51	409±25	134±18	12,0±0,4	7,3±0,68	—	10,8±0,8	18,3±1,2
1-1.5 min	10	508±37	157±24	14,3±1,2	6,8±0,6	—	13,6±1,3	16,6±1,4
15 "	11	358±56	144±24	14,1±0,8*	9,5±0,6*	—	15,7±1,6*	30,0±2,1*
45 "	12	251±13*	101±10	8,2±0,2*	5,4±0,36*	—	12,6±0,9	25,5±1,8*
100 "	9	285±16*	138±10	13,5±1,2	8,2±0,65	—	12,8±1,0	14,8±0,9*
12 h	10	266±19*	138±14	7,3±1,1*	3,8±0,31*	—	6,8±0,5*	12,1±0,7*
		Brain (without hypothalamic region)					Hypothalamus	
Normal	42	0,012±0,001	0,13±0,008	0,27±0,02	0,011±0,001	0,05±0,003	0,14±0,012	0,41±0,03
1-1.5 min	11	0,011±0,001	0,13±0,021	0,23±0,03	0,009±0,002	0,05±0,004	0,12±0,008	0,32±0,02*
15 "	8	0,007±0,001*	0,11±0,02	0,23±0,06	0,01±0,002	0,04±0,001	0,06±0,007*	0,55±0,03*
45 "	12	0,010±0,001	0,1±0,004*	0,29±0,01	0,006±0,001*	0,10±0,005*	0,12±0,01	0,25±0,02*
100 "	8	0,007±0,001*	0,08±0,003*	0,38±0,01*	0,008±0,001	0,05±0,002	0,27±0,012*	0,21±0,03*
12 h	11	0,010±0,001	0,11±0,008	0,22±0,02*	0,018±0,001*	0,05±0,006	0,09±0,006*	0,56±0,09

Note. * $P < 0.05$.

The decrease in the noradrenalin content in the hypothalamus 1.5, 45, and 100 min after injury was 25, 30, and 50%, respectively. According to some workers [1, 13, 14] the decrease in the noradrenalin reserves in the hypothalamus and reticular formation is one of the factors contributing to activation of the adrenal medulla. The results of the present investigation show that after head injury a decrease in the noradrenalin level is characteristic of all the brain tissues.

The decrease in the noradrenalin content in the brain does not reflect a decrease in its synthesis (this hypothesis is contradicted by the figures obtained for the content of precursors of the mediator [14, 20, 21]), but its inactivation by O-methylation under the influence of catechol-hydroxymethyl transferase, leading to elevation of the normetanephrine level in the central nervous system. Similar changes have also been demonstrated by other workers [16-19, 21].

Analysis of these results reveals the phasic character of changes in the catecholamines after head injury. During the first 15 min after injury, after an initial decrease in the noradrenalin level in the hypothalamus, the adrenalin system of the adrenals is activated, with the result that adrenalin is liberated from the adrenals into the blood stream (1st stage). The next stage (45 and 100 min after head injury) is characterized by a decrease in the reserves of adrenalin and of its precursors in the adrenals, restoration of the normal adrenalin level, and a decrease in the noradrenalin concentration in the blood. The noradrenalin level falls sharply in the brain tissue, especially in the hypothalamic region.

The lowered level of adrenalin and its precursors in the adrenals and blood 12 h after head injury indicates depression of the general activity of the adrenal medulla.

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