EFFECT OF AMPHETAMINE AND AMYTAL SODIUM ON BLOOD SEROTONIN LEVEL DURING STIMULATION OF THE HYPOTHALAMUS

É. É. Zvartau and A. Yu. Makarov

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Amphetamine (5 mg/kg) significantly lowers the serotonin concentration in venous blood draining from the brain. During hypothalamic stimulation after preliminary injection of amphetamine, there is a change in the direction of the swing in the serotonin concentration in the venous blood (instead of falling, as when the hypothalamus is stimulated before administration of amphetamine, its concentration rises). Amytal sodium (10 mg/kg) produced no regular changes in the serotonin concentration in the venous and arterial blood.

Reproduction of the behavioral and autonomic features of a diencephalic lesion in animals by electrical stimulation of the hypothalamus has revealed a correlation between changes in the serotonin concentration in the blood and CSF and the type of behavioral response [1, 2]. Characteristic changes in the serotonin level have been observed in patients with a hypothalamic syndrome during pharmacological tests with sympathomimetic and adrenomimetic drugs (amphetamine, adrenalin) and barbiturates [4].

The object of the present investigation was to study the effect of amphetamine and amytal sodium on the serotonin concentration in the biological fluids during experimental reproduction of the diencephalic syndrome.

EXPERIMENTAL METHOD

Serotonin was estimated in the blood plasma and CSF by a modification of Udenfriend's highly sensitive fluorometric method [3]. The lower limit of sensitivity of the method is about 1 ng/ml. Electrodes were implanted into various parts of the hypothalamus of 12 cats [2]. In a short experiment on animals immobilized with listhenon (2 mg/kg), four blood samples were taken from the jugular vein and carotid artery for serotonin estimation: 1) control; 2) after a series of 15 stimuli, 30 sec in duration, with an interval of 1.5 min between each (parameters of stimulation: square pulses, 1 msec, 100/sec, 0.5-3 V); 3) 30 min after intravenous injection of amphetamine (5 mg/kg) or amytal sodium (10 mg/kg); 4) after a second series of stimuli, similar to the first.

The serotonin level was determined in 13 intact cats before and after administration of amphetamine and amytal sodium in the doses given above; 5 control animals received no drugs, but the dynamics of the serotonin levels in the CSF and blood was investigated.

EXPERIMENTAL RESULTS

The serotonin concentration in venous blood of the 5 intact cats remained unchanged for 30-40 min, while in 1 animal the serotonin concentration in the arterial blood rose very slightly. Either no serotonin could be detected in the CSF of the intact cats, or its concentration was at the lower limit of sensitivity of the method.

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TABLE 1. Serotonin Concentration (in ng/ml) in Venous and Arterial Blood before and after Injection of Amphetamine

Statistical index	Venous blood		Arterial blood		Arterio-venous difference	
	before injection	after injection	before injection	after injection	before injection	after injection
$M \pm m$	31,12±7,50	11,63±2,30	33,15±6,14	30,60±8,30	—1,33	—13,81
P	<0,02		>0,05		>0,05	>0,05

TABLE 2. Effect of Hypothalamic Stimulation and Injection of Amphetamine on Serotonin Concentration (in ng/ml) in Venous Blood

Statistical index	Initial concn.	After 1st stimulation	After injection of amphetamine	After 2nd stimulation
$M+m$	36,07±1,10	23,66±1,98	21,73±4,50	39,61±6,55
P	<0,001		<0,02	

Amphetamine (7 experiments) caused a significant decrease in the serotonin concentration in the venous blood. A decrease in the serotonin level in the arterial blood was observed in 4 of 6 experiments, but on the average it was not statistically significant (Table 1). Amytal sodium had a less marked action: in 3 of 6 experiments the serotonin concentration in the venous blood was unchanged; on the whole the changes were not statistically significant. Neither drug altered the serotonin level in the CSF. Just as in the control cats, no serotonin was found in the CSF of these animals.

Hypothalamic stimulation after the previous administration of amphetamine caused a statistical increase in the serotonin concentration in the venous blood, whereas in response to stimulation without administration of amphetamine in this series of experiments the serotonin level in the venous blood fell (Table 2). Changes in the serotonin concentration in arterial blood under analogous experimental conditions were inconsistent in direction and not statistically significant. Stimulation of the hypothalamus after administration of amytal sodium gave rise to negligible or inconsistent changes in the serotonin concentration in both venous and arterial blood.

It will be noted that amphetamine lowered the serotonin concentration in blood draining from the brain, while repeated stimulation of the hypothalamus after preliminary administration of amphetamine changed the serotonin concentration in the venous blood in the opposite direction, and relatively more intensively than stimulation without administration of amphetamine. It is generally accepted that amphetamine exerts its effect through interference with catecholamine metabolism, although according to some reports amphetamine differs in its action on the metabolism of catecholamines and serotonin [5]. It follows from the present results that amphetamine promotes retention of serotonin in the brain tissues, and possibly for this reason more of it is liberated during hypothalamic stimulation.

Changes in the serotonin concentration after administration of amphetamine to patients with a hypothalamic syndrome and in response to electrical stimulation of the hypothalamus in experimental animals were consistent in direction, confirming the value of amphetamine loading as a nonspecific pharmacological test for the diagnosis of disturbances of hypothalamic function.

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