EFFECT OF AMPHETAMINE AND GUTIMIN ON ADAPTIVE CHANGES IN BLOOD PRESSURE DURING SKELETAL MUSCULAR CONTRACTION

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The effect of amphetamine and gutimin on the arterial pressure reflex to skeletal muscular contraction in response to stimulation of spinal ventral roots was investigated in acute experiments on decerebrate, unanesthetized cats. Doses of the drugs increasing locomotor activity and physical working capacity were used. Amphetamine in a dose of 0.1 mg/kg raised the systemic arterial pressure and the amplitude of the pressor reflexes. If the dose of amphetamine was increased to 1-11 mg/kg the pressor reflex was inhibited and the arterial pressure began to fall. Gutimin (5-50 mg/kg) raised the arterial pressure but did not affect the amplitude of the pressor response to skeletal muscular contraction.

KEY WORDS: arterial pressure; skeletal muscular contraction; amphetamine; gutimin.

The reflex elevation of the arterial blood pressure (BP) observed during muscular work [7, 10] has an adaptive role for it leads to an increase in the blood flow through the working muscles [5]. To what extent drugs increasing working capacity modify the adaptive BP reflex is not yet known although this has a direct bearing on the understanding of the mechanism of their action.

The object of this investigation was to study changes in the pressor reflex produced by amphetamine and gutimin in doses increasing locomotor activity and physical working capacity [1, 2, 9, 11, 12].

EXPERIMENTAL METHOD

Eighteen experiments were carried out on decerebrate cats. Decerebration was performed at the intercollicular level under ether anesthesia. Tetanic contractions of muscles of the right hind limb were evoked by stimulation of the peripheral ends of the divided ventral roots (L_6, L_7, S_1) of the spinal cord by supramaximal square pulses (50/sec, 0.1 msec, total duration of stimulation 10 sec). The interval between periods of stimulation was 15-20 min. The exposed area of the spinal cord and the stimulated roots were flooded with warm mineral oil. The strength of contraction of the triceps surae muscle was measured with the aid of semiconductor strain gauges under isometric conditions.

BP in the abdominal aorta was measured by an EMT-35 electromanometer (Elema-Schönander, Sweden). Respiration was recorded by means of a thermocouple in the tracheal cannula. All the indices studied were recorded on a "Mingograph-34" automatic recorder. During the experiment the animal was fixed in the SÉZh-3 stereotaxic apparatus and kept warm. The experiment began 1.5-2 h after administration of ether stopped. The drugs were injected intravenously in 0.5-1 ml physiological saline made up in bidistilled water.

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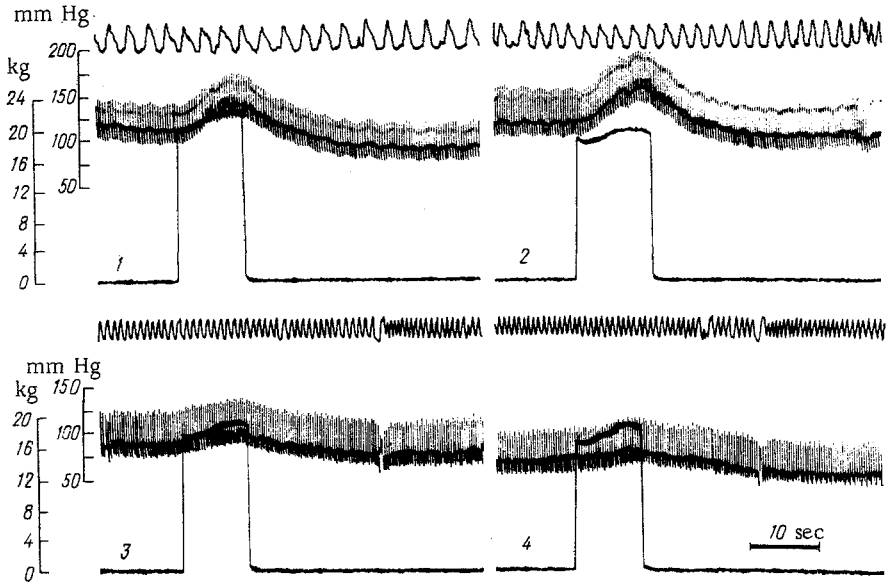

Fig. 1. Effect of increasing doses of amphetamine on amplitude of pressor reflex to contraction of hind limb muscles. Records from top to bottom: respiration, arterial blood pressure, strength of contraction of triceps surae muscle during stimulation of ventral roots L_6, L_7, S_1 (50/sec, 0.1 msec); 1) before injection; 2-4) during action of amphetamine in dose of 0.1 mg/kg (2), 1 mg/kg (3), and 6 mg/kg (4).

TABLE 1. Effect of Amphetamine and Gutimin on Systemic Arterial Pressure and Amplitude of Pressor Reflex Evoked by Contraction of Skeletal Muscles in Decerebrate Cats (M ± m)

Dose of substance (in mg/kg)	Exptl. conditions	Arterial pressure (in mm Hg)			Heart rate, beats/min	Respiration rate per min	Force of muscular contraction (in kg)
		systolic	diastolic	mean			
Before injection	I	127±10	76±6	93±4	205±16	25±2	
Amphetamine:	II	157±12	104±8	122±9	206±16	24±2	16,6±1,8
0,1	I	134±9	81±6	99±6	219±17	32±3	
	II	167±13	114±9	132±8	218±17	31±3	13,1±1,8
0,5	I	138±8	83±5	101±6	217±17	51±13	
	II	164±13	104±7	124±8	221±17	47±10	13,7±1,7
1,0	I	133±6	79±6	98±5	220±13	56±13	
	II	149±9	93±4	110±6	224±13	55±14	13,0±1,6
6,0	I	118±7	65±6	83±6	229±13	73±14	
	II	129±10	76±6	92±6	219±13	73±16	12,6±1,7
11,0	I	113±9	57±7	75±8	209±14	74±9	
	II	122±10	64±7	83±7	214±14	79±12	12,3±1,8
Before injection	I	115±8	70±10	85±9	200±7	20±3	
Gutimin:	II	143±14	100±13	114±13	200±6	25±8	13,6±1,7
5,0	I	122±8	78±10	93±6	184±10	22±5	
	II	149±9	105±10	119±10	187±12	26±8	13,3±1,5
20,0	I	132±10	89±9	104±9	170±15	22±4	
	II	158±10	114±9	128±9	172±16	25±8	12,1±1,7
50,0	I	136±4	94±4	107±3	168±9	26±5	
	II	160±10	118±9	131±6	173±10	27±8	11,3±1,8

Legend. I) Before, and II) during stimulation of ventral roots.

EXPERIMENTAL RESULTS AND DISCUSSION

Stimulation of the ventral roots of the spinal cord led to tetanic contraction of the hind limb muscles (Fig. 1) with a force of about 15 kg. The BP rose on the average by 29 mm Hg. The response of BP was purely reflex, for division of the ipsilateral dorsal roots or curarization of the animal caused the vascular response to disappear.

The effect of amphetamine on the pressor reflex depended on the dose of the drug (Table 1). In a small dose (0.1 mg/kg) amphetamine increased both the systemic BP level and the amplitude of the pressor response (on average by 15%). With an increase in the dose of the drug the amplitude of the pressor reflex induced by muscular contraction gradually diminished (Fig. 1). As a result of the action of amphetamine in a dose of 0.1 mg/kg the BP level at the height of the pressor reflex was 10 mm Hg higher than in the control. This increase of pressure must be regarded as considerable, for it appeared even in response to a weaker contraction of the muscles than in the control (during the experiment the power of the muscle decreased because of fatigue). In a dose of 0.1 mg/kg, amphetamine thus facilitates the adaptive pressor reflex and this must have a beneficial effect on the blood supply to the working muscles.

Elevation of BP and the increased amplitude of the pressor reflex to ventral root stimulation following a small dose of amphetamine are evidently attributable to the sympathomimetic action of the drug on postganglionic sympathetic nerve endings, for catecholamines are known not to facilitate the central components of sympathetic reflexes in decerebrate animals [3].

An increase in the dose of amphetamine was accompanied by a decrease in amplitude of the pressor reflex and a fall of BP (Table 1). The reduction of the adaptive shift of BP caused by musuclar contraction can presumably be attributed to the central sympathomimetic action of the drug. Drugs activating adrenergic mediation in sympathetic centers are known to depress short-latency (spinal) and long-latency (bulbospinal) sympathetic reflexes [8] and to lower the BP [6]. The results now obtained show that amphetamine potentiates the adaptive pressor reflex only in a small dose (0.1 mg/kg) with no effect on locomotor activity or working capacity. In doses of 0.5 mg/kg or higher, such as are usually used to increase working capacity, amphetamine impairs the "autonomic provision" for the skeletal muscles.

By contrast with amphetamine, gutimin caused practically no change in the amplitude of the pressor reflex during skeletal muscular contractions (Table 1). The decrease that was observed in this response was due to fatigue of the muscle and a reduction in the contraction developed by it. In control experiments (without the drug) a similar dynamics of changes in muscular force and the pressor reflex was observed. The absence of change in the pressor response through the action of gutimin points to the peripheral character of action of this drug [4].

Amphetamine and gutimin — substances increasing physical working capacity — thus differ in their effects on the adaptive shifts of BP arising in response to muscular activity. Amphetamine in a small dose facilitates the reflex but, in large doses, inhibits it. Gutimin, while raising the initial level on the BP, has virtually no effect on the amplitude of the pressor reflex, so that it could have a beneficial effect on the hemodynamics in the working muscle.

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