INHIBITION OF ELEVATION OF THE MONKEY PLASMA FATTY ACID LEVEL DURING STRESS BY ADMINISTRATION OF PROSTAGLANDIN

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Investigation of the level and composition of free fatty acids in the blood plasma of monkeys revealed definite changes after stress (immobilization) which were prevented by a single injection of prostaglandin E_2 immediately before exposure to the stressor. The role of prostaglandins as a factor in the feedback mechanism limiting the lipolytic effect of neuromediators and hormones, secreted intensively during stress, is analyzed.

KEY WORDS: stress, immobilization, lipolytic effect, prostaglandins.

The effect of various types of stress on lipolysis in adipose tissue and on the liberation of free fatty acids (FFA) into the blood is at present being widely investigated. These responses are attributed to the increased secretion of various hormones (corticosteroids, catecholamines) during stress with the invariable participation of the hypothalamic–pituitary system. Activation of a feedback mechanism during the development of lipolysis must be of great importance to the subsequent metabolic changes arising during stress.

It was recently shown that prostaglandins are liberated in response to stimulation of adrenergic nerves [7, 12]. It is postulated that prostaglandin E_2 (PGE_2) locally regulates the liberation of noradrenalin in the nerve ending, thus determining the duration of the effect of nerve stimulation [10, 11]. In the course of lipolysis induced by catecholamines, endogenous prostaglandins appear, lower the cyclic AMP level in fat cells, and inhibit the development of lipolysis [13].

The hypothetical role of prostaglandins in the regulation of the lipolytic effect [6] was the basis for the present investigation to study the effect of PGE_2 on the development of the raised blood fatty acid level in stress.

EXPERIMENTAL METHOD

Experiments were carried out on four monkeys (Papio hamadryas) aged 6-8 years, of both sexes, weighing 9.1-23.6 kg. Blood was taken from the cubital vein of the animals 12 h after feeding and their limbs were then fixed for 30 min to rigid supports [3]. Other monkeys moved about in the field of vision of the immobilized animals, arousing additional emotional stimulation [14]. Immediately after the experiment blood was again taken. The experiment was repeated 2 weeks later, but immobilization was preceded by intravenous injection of PGE_2 (1 μg/kg). Lipids were extracted from the blood immediately after taking the samples with a mixture of chloroform and methanol. Separation of the lipid fractions was carried

TABLE 1. Total FFA Concentration in Blood Plasma (in μmoles/liter) of Monkeys

Experimental conditions	Monkeys			
	№ 1	№ 2	№ 3	№ 4
Before immobilization	306	375	616	416
After immobilization	474	615	712	531
After immobilization + PGE_2	225	450	541	503

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TABLE 2. Changes in Individual FFA in Plasma (in %) of Experimental Monkeys

FFA	Monkeys											
	№ 1			№ 2			№ 3			№ 4		
	A	B	C	A	B	C	A	B	C	A	B	C
Saturated												
C_{12}	0,5	0,6	0,3	0,8	0,7	0,9	1,0	1,2	0,9	0,8	0,5	1,2
C_{13}	0,1	0,2	0,2	0,1	0,2	0,2	1,7	0,6	0,2	0,6	1,1	0,6
C_{14}	2,4	2,2	2,2	2,4	2,1	1,8	3,6	2,4	1,0	2,1	2,6	1,0
C_{15}	0,9	0,5	0,8	0,9	0,6	1,2	1,7	1,3	0,6	0,7	0,5	1,0
C_{16}	35,9	25,5	33,2	40,9	35,5	37,9	34,4	29,1	33,9	34,8	33,9	44,0
C_{17}	0,1	1,2	0,8	0,3	0,4	—	1,1	1,0	1,8	1,6	1,1	1,4
C_{18}	10,4	11,0	11,2	8,0	7,1	11,0	9,8	6,4	13,6	8,2	8,3	3,5
Total . . .	51,3	41,2	48,7	53,4	46,4	53,0	52,3	42,0	52,0	49,5	48,0	52,7
Unsaturated												
$C_{14:1}$	0,4	0,5	0,5	0,1	0,4	0,2	2,8	0,6	0,1	0,6	1,2	2,5
$C_{16:1}$	2,0	4,3	0,6	3,8	5,1	3,3	5,1	4,0	3,6	5,6	5,1	4,3
$C_{18:1}$	27,8	30,7	18,4	20,9	26,7	20,3	22,3	29,6	22,4	21,9	23,3	19,1
$C_{18:2}$	12,5	11,7	9,9	15,6	13,8	12,9	7,3	13,5	10,2	10,1	10,3	6,4
$C_{18:3}$	2,6	2,9	2,4	0,8	1,0	0,9	2,4	3,5	3,0	2,6	0,6	2,5
$C_{20:4}$	3,7	9,9	19,5	5,2	6,5	9,4	6,8	7,4	8,7	9,8	11,5	12,5
Total . . .	48,7	58,8	51,3	46,6	53,6	47,0	47,7	58,0	48,0	50,5	52,0	47,3

Legend: A) before immobilization; B) after immobilization; C) after immobilization +PGE_2.

out by chromatography on a thin layer of silicagel G (liquid-phase hexane : ether : acetic acid, 85 : 15 : 2.5). The FFA fraction was converted into methyl esters and passed through the GCHP 18 : 3 (VEB Chromatrom) gas chromatograph [1]. The total FFA content in the plasma also was determined [8].

EXPERIMENTAL RESULTS AND DISCUSSION

Stress led to a regular increase in the total plasma FFA concentration of the monkeys. A single injection of PGE_2 in a comparatively low dose before immobilization blocked this effect of stress (Table 1).

The level of saturated FFA fell and that of unsaturated rose in all the animals after immobilization. Stress in conjunction with PGE_2 administration did not change the relative content of saturated and unsaturated FFA in the plasma (Table 2).

The results in Table 2 show that PGE_2 restored the normal composition of the saturated FFA in the monkeys' plasma. However, this did not happen for the unsaturated FFA: although the level of most acids in stress accompanied by administration of PGE_2 remained normal or fell, the content of arachidic acid ($C_{20:4}$), on the contrary, increased more than it did during immobilization without PGE_2.

The fall in the plasma FFA concentration under the influence of PGE_2 agrees with data in the literature [4, 5, 18]. The results evidently confirm the view that PGE_2 prevents the manifestation of the lipolytic effect of noradrenalin and other hormones whose liberation is increased during stress. Hence it follows that the lipolytic effect of stress depends not only on the effect of catecholamines but also on their interaction with other biologically active compounds. In particular, in the presence of ACTH and adrenocortical hormones the sensitivity of triglyceride lipase to noradrenalin is increased [16, 17].

The fact that prostaglandins of the E group prevent the lipid-mobilizing action of catecholamines may indicate that the prostaglandins themselves are the factor liberated during stimulation of adrenergic nerves in accordance with the feedback mechanism, to restrict the effect of lipolytic agents [12, 15]. Infusion of PGE_1 and PGE_2 has been shown to reduce the quantity of noradrenalin liberated on stimulation of adrenergic nerves [10, 11]. The present experiments demonstrate the effect of PGE_2 in preventing the manifestation of a lipolytic response to stress and preventing a change in the FFA composition that could lead to the development of further disturbances in metabolism during stress. Elevation of the plasma arachidic acid level under the influence of PGE_2 agrees with earlier observations on the action of high doses of PGE_1 [2].

The results indicate that prostaglandins help to maintain the level and composition of the blood FFA within normal limits and to prevent the sharp fluctuations in them that arise during stress. These findings may help to elucidate the biological role of prostaglandins and also the mechanisms controlling lipolysis under physiological and pathological conditions.

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