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G. G. Khechninashvili

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ROLE OF ADRENALS IN THE MOBILIZATION OF CARBOHYDRATE AND FAT RESOURCES AFTER OVERSTIMULATION OF RATS

By G. G. Khechinashvili, Group of Neural-Endocrinology (Head--Doctor of Medical Sciences V. Ye. Ryzhenkov), Department of Pharmacology (Head--Academician of USSR Academy of Medical Sciences, Professor S. V. Anichkov) of the Institute of Experimental Medicine of the USSR Academy of Medical Sciences, Leningrad

Adrenodemedullation and adrenalectomy in rats greatly hampers the rise of the blood plasma glucose concentration in response to immobilization. The liver glycogen content subsides in these animals to a much greater degree than in intact ones. Adrenodemedullation and adrenalectomy do not eliminate the adipokinetic action of immobilization. In mobilization of the blood sugar following extraordinary irritation (overstimulation) of rats, the leading part is played by the secretion of the adrenal medullary layer, whereas the role of suprarenals in the mobilization of fats is only slightly pronounced.

Glucose and free (nonesterified) fatty acids (FFA -- free fatty acids) /575* are the main energy resources of the organism. Their mobilization respectively from glycogen of the liver and triglycerides of the fatty depots when the organism is affected by stimulants has been established by a number of authors (Selye, 1950; Engel and Fredericks, 1957; S. M. Leytes and Chzhou-su, 1962; Friedberg et al., 1963; V. Ye. Ryzhenkov et al., 1968; N. G. Nikul'cheva and V. Ye. Ryzhenkov, 1970). The participation of the sympathetic nervous

*Numbers in margin indicate pagination in original foreign text.

system, adrenalin of the adrenal glands and a number of other hormonal factors is assumed in the mechanism of these reactions (Havel and Goldfien, 1959; Shafrir et al., 1960; S. M. Leytes and Chzhou-su, 1962; Lebowitz, 1965; Goodman, 1969; N. G. Nikul'cheva and V. Ye. Ryzhenkov, 1970; Goth, 1971). The question of the value of secretion of the adrenal gland in these processes has been studied much less.

In this work a study was made of the role of the cortical and cerebral layers of the adrenal glands in mobilizing carbohydrate and fatty resources in response to the effect of an extreme stimulant. Immobilization of rats was used as the latter; as is known immobilization produces considerable change in the activity of the nervous and endocrine systems and results in a whole series of biochemical changes in the organism (Brodie and Hunson, 1960; S. V. Anichkov and I. S. Zavodskaya, 1965; V. Ye. Ryzhenkov, 1968 et al.).

Methods of Study /576

The experiments were conducted on 350 satiated male rats weighing 180-200 g. The animals were immobilized by fixing them in a stand for different periods: 10, 30 minutes, 1 and 3 hours. Immediately after immobilization the rats were decapitated. The concentration of total 11-hydroxycorticosteroids (11-HXC) in the blood plasma was determined fluorometrically (I. Ya. Usvatova and Yu. A. Pankov, 1968), free fatty acids in the plasma--by the colorimetric method (Itaya and Ui, 1965), glucose in the plasma--also colorimetrically: by the glucose-oxidase and for comparison the ortho-toluidine methods (E. G. Tebneva and G. I. Saburova, 1970). The glycogen in the liver was analyzed

by a modified iode method of Krisman (I. V. Vysochina et al., 1968). Adrenalectomy was carried out 36-48 hours before the experiment. After adrenalectomy the rats received 1% solution of sodium chloride to drink. A number of the animals were given minimum doses of hormones (directly before the operation 2.5 mg/kg of desoxycorticosterone-acetate (DOCA) intramuscularly, one hour before the experiment 2.5 mg/kg DOCA, and 25 g/kg of dexamethasone intraabdominally). Another part of the adrenalectimized rats entered the experiment without supporting therapy. Demedullation of the adrenal glands was carried out one month before the experiment by removal of the cerebral layer with a special spoon. Complete removal of the cerebral and preservation of the cortical layers of the adrenal glands were checked histologically after the experiments. The results of the experiments were statistically processed (M. L. Belen'kiy, 1963).

Results and Their Discussion

The table presents the studied indices of carbohydrate and fatty metabolism after different periods of immobilization in the intact and operated on animal and rats who were given DOCA and dexamethasone.

It is apparent that the hyperglycemic reaction to immobilization in the intact rats developed already in the early periods of stimulation (10 minutes) and the concentration of glucose in the blood plasma was high during all the studied periods of immobilization. This was accompanied by intensified glycogenolysis in the liver. The glycogen content in the liver was progressively reduced with an increase in the periods of immobilization.

TABLE. EFFECT OF ADRENODEMEDULLATION AND ADRENALECTOMY ON MOBILIZATION OF CARBOHYDRATES AND FATS DURING STIMULATION OF RATS

Group of Animals		Glucose of plasma (in mg%)		Glycogen of liver (in g%)		Fatty acids of plasma (in equiv/l)	
		$M \pm m$	P	$M \pm m$	P	$M \pm m$	P
Intact	Control	117,9±3,7 (12)		4,09±0,21 (9)		462,5±17,8 (19)	
	Imm. 10 minutes	181,4±8,2 (15)	<0,001	3,26±0,26 (7)	<0,05	599,1±20,3 (23)	<0,001
	Control	130,2±2,2 (33)		3,81±0,28 (9)		426,7±14,6 (16)	
	Imm. 30 minutes	207,9±3,8 (37)	<0,001	3,22±0,22 (8)	<0,05	595,2±24,6 (18)	<0,001
	Control	127,4±2,6 (16)		4,26±0,23 (8)		427,7±18,3 (13)	
	Imm. 1 hour	211,7±4,8 (16)	<0,001	2,61±0,19 (7)	<0,01	600,3±27,7 (13)	<0,001
	Control	131,4±2,8 (11)		5,06±0,38 (6)		437,0±15,8 (17)	
	Imm. 3 hours	198,6±5,1 (9)	<0,001	1,70±0,30 (6)	<0,001	833,2±17,6 (17)	<0,001
Those who received DOCA[1]	Control	139,1±3,0 (8)				415,5±27,3 (4)	
	Imm. 30 minutes	208,4±11,8 (8)	<0,001			556,6±37,2 (4)	<0,05
Those who received dexamethasone	Single administration[2] Control	153,5±3,4 (12)					
	Imm. 30 minutes	252,3±13,4 (12)	<0,001				
	Two-fold administration[3] Control	167,4±8,9 (10)		7,87±0,45 (5)		894,6±41,4 (6)	
	Imm. 30 minutes	315,1±14,5 (10)	<0,001	5,55±0,47 (5)	<0,05	1011,6±41,4 (6)	>0,05
	With substitution administration of hormones (for doses see the text) Control	106,4±4,1 (5)				399,0±13,1 (5)	
	Imm. 10 minutes	123,4±3,8 (5)	<0,05			526,3±22,7 (5)	<0,01
	Control	118,7±4,0 (5)				414,4±16,6 (5)	
	Imm. 30 minutes	131,6±2,6 (5)	<0,05			528,7±14,6 (5)	<0,01
Adrenalectomized	Control	130,7±5,7 (5)				381,2±9,2 (5)	
	Imm. 1 hour	144,0±2,8 (5)	>0,05			558,4±35,4 (5)	<0,01
	Control	129,1±3,3 (5)				357,0±19,3 (5)	
	Imm. 3 hours	111,2±4,4 (5)	<0,05			664,4±32,3 (5)	<0,001

[continuation of table]

Group of Animals		Glucose of plasma (in mg%)		Glycogen of liver in g%)		Fatty acids of plasma (in equiv/l)	
		M±m	D	M±m	D	M±m	D
Without substitution administration of hormones	Control Imm. 10 minutes	115,1±4,1 (6) 120,5±2,6 (6)	>0,05	2,44±0,32 (6) 1,85±0,18 (6)	>0,05	411,2±30,2 (5) 585,5±43,6 (5)	<0,05
	Control Imm. 30 minutes	127,7±4,6 (7) 153,1±3,1 (7)	<0,01	2,69±0,27 (7) 1,88±0,38 (6)	>0,05	437,4±9,6 (5) 627,5±11,0 (5)	<0,001
	Control Imm. 1 hour	118,8±3,5 (5) 135,8±2,9 (5)	<0,05	2,57±0,27 (5) 1,33±0,24 (5)	<0,01		
	Control Imm. 3 hours	130,5±4,3 (5) 60,9±6,3 (7)	<0,001	3,03±0,14 (5) 0,16±0,02 (7)	<0,001	372,4±23,9 (5) 762,9±33,5 (5)	<0,001
Adrenodemedullized	Control Imm. 10 minutes	135,2±8,0 (4) 155,4±6,8 (4)	>0,05	5,02±0,65 (4) 3,10±0,38 (4)	>0,05	410,3±47,6 (4) 426,5±16,0 (4)	>0,05
	Control Imm. 1 hour	138,8±9,8 (4) 133,8±10,0 (4)	>0,05	4,70±0,80 (4) 1,31±0,05 (4)	<0,05	386,2±32,2 (4) 671,0±51,5 (4)	<0,01
	Control Imm. 3 hours	129,1±5,7 (4) 89,8±6,4 (4)	<0,01	4,23±0,43 (4) 0,44±0,07 (4)	<0,001	400,9±25,3 (4) 332,5±89,2 (4)	<0,01

Notes: 1. In parentheses the number of animals in the group is given
2. Imm.—immobilization

Footnote 1. DOCA12.6 mg/kg intramuscularly 18 hours before experiment and 12.5 mg/kg intraabdominally 2 1/2hours before 30 minute immobilization
2. Dexamethasone1 mg/kg intraabdominally 2 1/2 hours before 30 minute immobilization
3. Dexamethasone0.8 mg/kg intraabdominally 48 hours before experiment and 0.5 mg/kg intraabdominally 2 1/2 hours before 30 minute immobilization

As follows from the table adrenodemedullation and adrenalectomy to a considerable degree disrupted the hyperglycemic reaction to the extreme stimulation. A tendency was merely noted for an increase in the sugar content in the blood plasma in the early periods of immobilization, which apparently was linked to the extra-adrenal activity of the sympathetic nervous system (S. M. Leytes and Chzhou-su, 1962). In the experiments on the adrenalectomized animals without substitution administration of small doses of corticosteroids it was established that after 3-hour immobilization there was considerable reduction in the concentration of sugar in the plasma. In the adrenalectomized rats maintained with small doses of hormones this effect of mobilization was considerably less pronounced (see table). Similar action of the corticosteroids administered to the adrenalectomized rats has already been noted in the literature (Engel and Fredericks, 1957).

That fact that suppression of the hyperglycemic reaction to the stimulus was observed not only in the adrenalectomized, but also in the adrenodemedullized animals indicates the leading role of secretion of the cerebral layer of the adrenal glands in increasing the level of sugar in the plasma.

In the operated on (especially the adrenalectomized) animals as compared to the intact during prolonged immobilization a considerably more pronounced decrease was observed in the glycogen content in the liver, almost complete exhaustion of the carbohydrate supplies. Similar results were obtained previously in our section (V. V. Korkhov, 1970). It should be noted that adrenalectomy reduced also the initial level of glycogen in the liver, while during demedullation of the adrenal gland such an effect was not noted (see

table). Apparently this is explained by the action of the glucocorticoids on neoglucogenesis. The latter is confirmed by the results of our experiments with administration of synthetic glucocorticoid dexamethasone to intact animals, as well as by the experiment to investigate the 11-HXC content in the blood plasma.

As is apparent from the table the administration of dexamethasone to /579
intact animals resulted in the increase in the initial concentration of glucose in the plasma and intensification of the hyperglycemic reaction to immobilization. Two-fold administration of dexamethasone was accompanied also by a considerable increase in the glycogen content in the liver and a certain reduction in the degree of its decrease during immobilization.

A distinct increase in the 11-HXC level in the plasma was observed already by 10 minutes of immobilization in which the maximum by 30 minutes. The 11-HXC level in the plasma remains high even in the later periods of immobilization. In the adrenodemedullized animals the reaction of the adrenal cortex to immobilization was as well pronounced as in intact (see the figure). Administration of mineral-corticoid dezoxycorticosteroid did not reproduce any of the studied effects of dexamethasone (see table).

The concentration of free fatty acids in the plasma of intact rats exposed to immobilization, in the same way as glucose, increased already in 10 minutes. In contrast to the concentration of sugar in the plasma it sharply increased after 3-hour stimulation. This lipo-mobilizing effect was not significantly altered either by adrenodemedullation or adrenalectomy (see table). In the adrenalectomized rats who received a supporting dose of

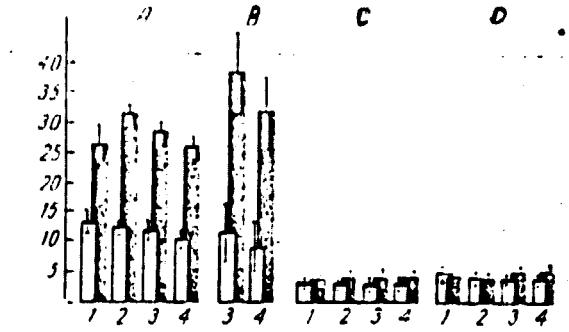

Figure. Effect of Different Periods of Immobilization on Level of Total 11-Hydroxycorticosteroids (11-HXC) in Plasma of Intact (A), Adrenodemedullized (B) and Adrenalectomized Rats Without Administration of Hormones (C) and After Administration of Hormones (D).

On vertical--concentration of 11-HXC (in μg%). Light columns--control; dark--after immobilization for 10 minutes (1), 30 minutes (2), 1 hour (3), 3 hours (4), confidence boundaries computed with D=0.05. A--in control and experimental groups of 20 animals; B, C, D--5 animals

DOCA and dexamethasone and in the animals that did not receive these hormones the differences in the liver of the adipokinetic reaction to the employed effect was not observed.

The lipo mobilizing effect of immobilization was implemented, apparently, as a result both of the increase in the activity of the sympathetic nervous system (Havel and Goldfien, 1959 et al.), and the extra-adrenal lipolytic effect of ACTH (Lebowitz and Engel, 1965; Lebowitz, 1965; N. G. Nikul'cheva and V. Ye. Ryzhenkov, 1970; Desbals et al., 1970), and possibly with the participation of other hormonal factors (Goodman, 1969; Goth, 1971).

Thus, the results of the conducted experiments indicated that in implementing the hyperglycemic reaction emerging during immobilization of rats

the leading role belongs to secretion of the cerebral layer of the adrenals. Here the value is revealed of the cortical layer of the adrenal glands since injection of small doses of corticosteroids prevents the pronounced decrease in the glucose role in the blood plasma observed in adrenallectomized rats after 3-hour immobilization.

In mobilization of the fatty resources the role of the adrenals is less pronounced. Despite the well known lipolytic action of adrenalin (Havel and Goldfien, 1959; Goodman, 1969 et al.), as well as the fact that injections of dexamethasone resulted in a considerable increase in the FFA content in the blood plasma (see table), in our experiments the adipokinetic action /580
of immobilization was observed both in the adrenodemedullized and in the adrenalectomized animal. However in the implementation of this effect in the adrenalectomized rats that residual quantity of corticosteroids that was recorded in the blood plasma in our experiments 1 1/2-2 days after removal of the adrenal glands could have a permissive effect.

Conclusions

1. A leading role in the hyperglycemic reaction to an extreme stimulus belongs to the secretion of the cerebral layer of the adrenal glands.

2. Injections of dexamethasone result in considerable increase in the content of free fatty acids in the blood plasma. At the same time the adipokinetic effect is well pronounced in immobilization both in adrenodemedullized and adrenalectomized rats.

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