has been described in other models (the principle of the dual functional burst) [1]. Just as in cases of generators of pathologically enhanced excitation (GPEE) formed during a disturbance of inhibitory control in other CNS structures [1], the character of changes arising in epileptide cortical structures receiving the burst depends on the degree of disturbance of inhibition and of lowering of the thresholds of excitability in these structures. If a sufficient degree of effectiveness of inhibitory neurons is preserved in the epileptic focus, the incoming impulsation during stimulation of DN activates these neurons and causes suppression of the focus. During a considerable disturbance of inhibition and lowering of the thresholds of excitability of the neurons in the focus, however, impulsation from DN may cause increased activity of the epileptic focus. Support for this mechanism is given by the fact that ES of DN causes inhibition of activity in the zone where secondary conducted activity, induced by the determinant focus, was recorded, i.e., where inhibitory mechanisms were preserved. With a fall in the intensity of epileptic activity (with the course of time and during continued sessions of ES), however, i.e., during restoration of the inhibitory mechanisms, ES of DN suppresses epileptic activity.

The results thus indicate the great importance of the dentate nucleus of the cerebellum as part of the antiepileptic system of the brain in suppression of epileptic activity in the neocortex.

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DYNAMICS OF BLOOD TYROSINE LEVEL IN ADRENALECTOMIZED AND INTACT RATS EXPOSED TO STRESS

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UDC 612.453.018-06:613.863]-08:612.124:547.587.42

KEY WORDS: tyrosine; immobilization stress; adrenal cortex.

The reserve powers of the adrenal cortex in clinical practice are usually estimated by studying changes in the blood and (or) urinary levels of corticosteroid hormones after admin-

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(Presented by Academician of the Academy of Medical Sciences of the USSR I. P. Ashmarin.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 95, No. 3, pp. 29-31, March, 1983. Original article submitted August 26, 1982.

0007-4888/83/9503-0286$07.50

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istration of ACTH preparation. However, the rate of secretion of corticosteroid hormones and their concentration in the biological fluids of normal subjects vary within wide limits both in a state of physiological rest and during ACTH loading, and this makes it more difficult to interpret the data [7, 10]. In stress situations and in various diseases the corticosteroid level in the blood and urine varies even more considerably [9]. Moreover, determination of corticosteroid levels in patients receiving corticosteroid preparations does not give a correct idea of adrenocortical function, not to mention the fact that ACTH cannot be given to seriously ill and enfeebled patients. Various adverse circumstances could prohibit the use of an indirect parameter, directly dependent on glucocorticoids and providing a measure of saturation of the body with these hormones. One such parameter is the blood level of tyrosine, for, because of the distinctive features of catabolism of this amino acid, it is determined chiefly by activity of liver tyrosine aminotransferase (TAT; EC 2.6.1.5), which is directly proportional to the quantity of glucocorticoids entering the liver [3]. Injection of glucocorticoid preparations, which stimulate TAT synthesis, causes the blood tyrosine level in man and animals to fall [8, 12]. A deficiency of glucocorticoids in the body, however it may arise, must be manifested as elevation of the blood tyrosine level [4]. This hypothesis has been confirmed for a state of physiological rest, in endocrine pathology, namely congenital virilizing dysfunction of the adrenal cortex in children [6], and during dynamic observation after bilateral adrenalectomy in rats [5].

The object of the present investigation was to study whether the time course of the blood tyrosine concentration can be used to characterize the state of the adrenocortical reserves.

EXPERIMENTAL METHOD

Both adrenals were removed from male albino rats weighing 115-120 g through a dorsal incision under ether anesthesia. On the 10th day after adrenalectomy the rats were subjected to immobilization stress — they were fixed in recumbency, in the supine position, for 30 min and 4 h. The control to each series of experiments consisted of intact rats of the same batch. Immediately before the 4-h period of immobilization, the group of adrenalectomized rats was given an intraperitoneal injection of hydrocortisone (from Gedeon Richter, Hungary) in a dose of 50 mg/kg body weight.

The tyrosine concentration was determined spectrophotometrically by the method in [14] in blood samples taken from the tip of the tail immediately before immobilization and 4, 8, and 22 h after the beginning of exposure to stress. The 11-HCS concentration was determined by the method in [1] on a fluorometer (from Hitachi, Japan) in blood samples taken before and 30 min and 4 h after the beginning of exposure to stress. The determination was made on a pool of sera from five animals, the volume of which was not less than 0.5 ml.

EXPERIMENTAL RESULTS

Judging from their behavior, rats not undergoing operation tolerated immobilization well, whether for 30 min (11 rats) or for 4 h (13 rats). Nine adrenalectomized rats were immobilized for 30 min. Eight of these animals tolerated the load well, but one rat died 2 h after the end of exposure. Of the 20 adrenalectomized rats exposed to immobilization for 4 h five animals died during 3-7 h after the beginning of exposure, 13 died between 12 and 22 h thereafter, and two rats survived and their condition was good after 24 h. Blood was taken from dying rats by decapitation. Of the group of adrenalectomized rats receiving hydrocortisone, five animals tolerated immobilization for 4 h well.

The blood 11-HCS level of the intact rats before the beginning of exposure was 20.4 μg/100 ml, after immobilization for 30 min it was 68 μg/100 ml, and 4 h after the beginning of exposure it was 31.5 and 32.5 μg/100 ml, respectively, in rats immobilized for 30 min and 4 h. The initial 11-HCS level in the adrenalectomized rats was 8.7 μg/100 ml, whereas 30 min and 4 h after the beginning of exposure the 11-HCS concentration was not determined after either short-term or long-term immobilization.

The tyrosine level before the beginning of exposure to stress was on average the same in the intact and adrenalectomized rats: in different series of experiments it ranged from 17.4 ± 4.8 to 23.6 ± 2.6 μg/ml. The initial tyrosine concentration in each experimental group is taken as 100% in Fig. 1 and its fluctuations in the course of the experiment are represented as percentages of the corresponding initial value.

In intact rats immobilized for both periods a gradual fall in the tyrosine level was observed, to reach about half of the initial value after 22 h. The tyrosine level was raised in adrenalectomized rats after fixation for 30 min, but it returned to its initial value after 22

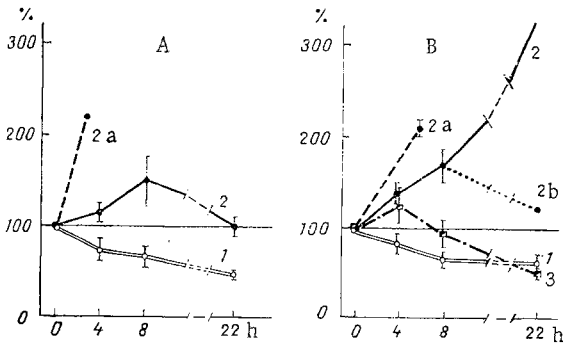

Fig. 1. Dynamics of blood tyrosine level in rats immobilized for 30 min (A) and 4 h (B). A: 1) Tyrosine level in intact rats, 2) in adrenalectomized rats (eight animals), 2a) in rats dying 2 h after the end of exposure. B: 1) Tyrosine level in intact rats, 2) in adrenalectomized rats dying in the course of 12-22 h after the beginning of stress (13 animals), 2a) in adrenalectomized rats dying 3-7 h after the beginning of stress (five rats), 2b) in two adrenalectomized rats which survived immobilization for 4 h, 3) in adrenalectomized rats receiving hydrocortisone. Abscissa, time after beginning of exposure (in h); ordinate, tyrosine concentration (in %).

h. The dynamics of the blood tyrosine level in adrenalectomized rats after immobilization for 4 h differed depending on the outcome of exposure: in animals which died it rose rapidly, but in rats which survived, after a temporary rise it returned almost to its initial level 22 h later. Differences in the outcome of exposure to stress of adrenalectomized rats for 4 h could evidently be attributed to differences in the degree of activation of accessory adrenal tissue [11]. The tyrosine level in adrenalectomized rats receiving hydrocortisone was raised a little after 4 h, probably because of absence of the necessary concentration of the preparation in the liver 30 min after the beginning of exposure [2], at the peak of the adrenocortical response of the intact animal [14]. The tyrosine concentration later fell, to repeat its time course in the intact animals.

Exposure of intact rats to stress thus caused the blood tyrosine level to fall, whereas in rats with adrenal insufficiency it rose. In the case of moderate exposure to stress this rise was transient, but in the case of severe stress, leading to death of the animals, a sharp increase in the tyrosine level was observed. The transient rise in the blood tyrosine level of rats after moderate exposure to stress can evidently be regarded as a manifestation of insufficiency of the adrenocortical reserves, and this could be responsible for the deaths arising as a result of more severe exposure.

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