CHANGES IN CATECHOLAMINE LEVELS IN BRAIN NUCLEI OF RATS WITH IMMOBILIZATION STRESS

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UDC 612.822.2:577.175.52]-06:
613.863-02:612.766.2

KEY WORDS: immobilization stress; aftereffects; dopa; catecholamines; brain nuclei; locus coeruleus + n. subcoeruleus; substantia nigra.

Exogenous or endogenous emotional stimuli give rise to considerable neurochemical and neurophysiological changes that form a special functional state of the brain characteristic of emotional stress (ES) [2].

An essential correlate of ES is a shift of the catecholamine (CA) levels in the brain and other organs, connected with significant metabolic, structural, and functional changes not only in formations synthesizing CA, but also in structures innervated by CA-containing fibers.

In the study of the mechanisms of stability of physiological functions during ES it is important to know how long after ES the changes in the CA concentration in the brain nuclei caused by it will last and, consequently, how long the structures will be exposed to particular metabolic and functional deviations.

The aim of this investigation was to study the time course of the CA concentration in the principal noradrenalin-synthesizing nuclei of the brain stem — the locus coeruleus + n. subcoeruleus (l.c. + n.sc.) and the mesencephalic dopamine-synthesizing nucleus — the substantia nigra (s.n.) at different times after immobilization stress.

EXPERIMENTAL METHOD

Experiments were carried out on 30 male Wistar rats weighing 250-300 g. ES was produced by immobilization (IM) of the animals on a board with the limbs and head securely fixed [3] for 2 days, in three sessions with intervals. On the first day the rats were immobilized from 10 a.m. to 3 p.m., after a rest of 2 h they were again fixed to the board and left overnight. Next morning IM was discontinued until the evening. The animals were again immobilized at 5 p.m. on that day until next morning.

Animals of group 1 were decapitated immediately after the end of IM, those of group 2 after 15 days, and those of group 3 after 30 days. Animals which were not immobilized but kept under the same conditions in the animal house served as the control. All the animals were killed at the same time — between 9 and 11 a.m.

The brain was quickly removed, frozen on dry ice, and frozen sections 300 μ thick were cut. The corresponding nuclei were expressed by the punching method [7]: i.c. + n.sc. were assessed together, the mean weight of the sample, like that of s.n., being 1 μg.

Concentrations of CA (adrenalin, noradrenalin, and dopamine separately) and also of dopa were determined by high-efficiency liquid chromatography on the LC-154 instrument with an electrochemical detector (from BAS, USA).

The significance of differences between the control and experiment was estimated by a t test.

EXPERIMENTAL RESULTS

The time course of the dopa and CA levels in l.c. + n.sc. and s.n. differed, as was shown primarily by the absence of any changes in the levels of these substances compared

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 0007-4888/86/0011-1494$12.50

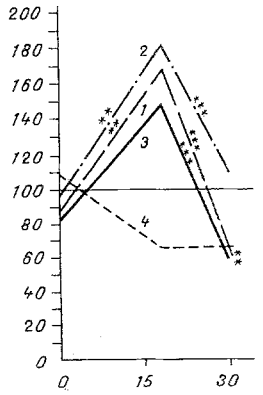

Fig. 1

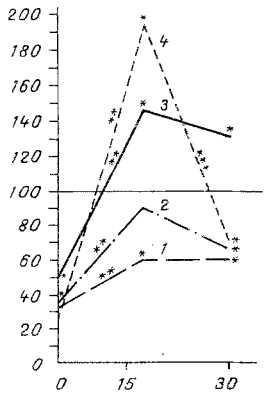

Fig. 2

Fig. 1. Changes in CA concentration in s.n. at different times after ending of IM. Abscissa, time after IM (in days); ordinate, change (in % of normal). Horizontal line — normal. 1) Dopa; 2) dopamine; 3) noradrenalin; 4) adrenalin. *) Differences significant compared with normal; **) differences significant beweeen groups 1 and 2; ***) between groups 2 and 3.

Fig. 2. Change in CM concentration in l.c. + n.sc. at different times after end of immobolization. Legend as in Fig. 1.

with the control immediately after IM in s.n., whereas in l.c. + n.sc. a significant decrease in the concentration of total CA and dopa was found at this time (Figs. 1 and 2).

We know that the CA concentration in individual brain nuclei changes after a single episode, even if short in duration, of immobilization stress [1, 4-6, 8-12]. It can be tentatively suggested that under the experimental conditions used the CA and dopa levels in s.n. returned ot their initial values by the end of IM, whereas in l.c. + n.sc. they remained (with, perhaps, some fluctuations) below the control values. Incidentally, under identical experimental conditions the range of fluctuations of the CA concentrations was much greater in l.c. than in s.n. [1]. The CA level in the brain nuclei, including in s.n., also changed differently depending on the time course of the physiological functions in stress [1]. All these factors could influence the dopa and CA concentration after IM.

An increase in the concentrations of CA and dopa was found 15 days after the end of IM, in both s.m. and l.c. + n.sc., compared either with the preceding period (dopamine in l.c. + n. sc. and noradrenalin in s.n.) or with the control and the previous period (adrenalin and noradranalin in l.c. + n.sc., dopamine in s.n., dopa in both structures). It can be tentatively suggested that the increase in the concentrations of dopa and CA was due to mechanisms similar to those observed during repeated stress. It has been shown that during repeated stress the raised concentration of CA and their increased turnover and synthesis are achieved through an increase in the number of tyrosine hydroxylase molecules, for this enzyme is regarded as one factor of long-term adaptation to repeated stress [4, 8].

Comparison of the data in Figs. 1 and 2 shows that the levels of dopa and dopamine in l.c. + n.sc. 15 days after the end of IM are raised only compared with the previous period, whereas in s.n. they are raised compared with the control also. One possible cause of the low dopa and dopamine concentrations in l.c. + n.sc. is their utilization for increased noradrenalin synthesis, the intensity of which is almost 1.5 times higher in these structures 15 and 30 days after IM than in the control.

Like l.c., s.n. receives terminals of axonal branches of adrenalin-synthesizing neurons from region A_1, but s.n. receives fewer of them than l.c. [13]. This is responsible for the lower initial adrenalin level in s.n. than in l.c. + n.sc. in these experiments (0.25 ± 0.04 and 0.9 ± 0.09 ng/mg tissue respectively) and also, possibly, for the absence of any significant changes in the adrenalin level after IM in s.n.

Concentrations of dopa, dopamine, and noradrenalin in s.n. 30 days after the end of IM were sharply reduced compared with the previous time (15 days). Conversely, the concentrations of dopa and the above-mentioned CA in l.c. + n.sc. remained at virtually the same

level. The sharply increased noradrenalin concentration in l.c. + n.sc. suggests maintenance of a high level of CA synthesis in the noradrenalin-synthesizing nuclei. Noradrenalin is released in s.n. from endings of incoming axons of noradrenalin-synthesizing neurons. The data in Figs. 1 and 2 indicate a different time course of the noradrenalin level in l.c. + n.sc. and s.n., in agreement with data in the literature showing definite differences in CA secretion in bodies of neurons and terminal ramifications of their axons [9].

For 30 days after the end of IM significant changes thus take place in dopa and CA levels in the noradrenalin-synthesizing nuclei of the brain stem (l.c. + n.sc.) and the mesencephalic dopamine-synthesizing nucleus (s.n.). The most marked changes affect the noradrenalin concentration in l.c. + n.sc.: By the 30th day it still remains almost 1.5 times higher than in the control. Survival of the animals after long-term IM suggests that the raised level of noradrenalin in the noradrenalin-synthesizing nuclei of the brain stem under these experimental conditions is protective in character.

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PEPTIDERGIC ASYMMETRY OF THE RAT SPINAL CORD

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UDC 612.83.18:577.175.82]-088.1

KEY WORDS: spinal cord; peptides; naloxone; lateralization; spinal memory.

Neurochemical studies of the brain have shown that dominance of one of the paired structures may be due to pre-existing or acquired asymmetry of distribution of endogenous chemical regulators and, in particular, of mediators and their receptors [8, 9]. There are hardly any data on the neurochemical lateralization of the spinal cord. Yet such data are extremely important for an understanding of the mechanisms of asymmetrical responses of the spinal cord to the action of chemical compounds [1-7].

The aim of this investigation was to study the effect of extracts of halves of the spinal cord (the lumbosacral enlargement) on muscle tone in the hind limbs of rats, changes in the effect of extracts of the whole lumbar division after selective activation of neurons in its right half, and the chemical nature of lateralization factors (LF), which are substances causing asymmetrical changes of muscle tone in the hind limbs.

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(Presented by Academician of the Academy of Medical Sciences of the USSR D. S. Sarkisov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 102, No. 11, pp. 528-530, November, 1986. Original article submitted March 13, 1986.

0007-4888/86/0011-1496$12.50