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EFFECT OF β-ENDORPHIN AND DELTA SLEEP-INDUCING PEPTIDE ON RESISTANCE TO EMOTIONAL STRESS

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Resistance to emotional stress depends on genetic and individual factors [1, 5, 8-10]. Wistar rats have been shown to be most resistant to emotional stress, whereas August rats are least resistant. Endogenous peptides (substance P, delta sleep-inducing peptide – DSIP) significantly increase the resistance of animals to emotional stress [6, 7, 9, 10]. Intravenous injection of DSIP lowers the blood pressure of spontaneously hypertensive rats [12]. Opioid peptides also have been shown to participate in the mechanisms of emotional reactions [11, 13, 14]. It is therefore interesting to study the role of endogenous peptides in mechanisms of emotional reactions in rats differing in their genetically determined resistance to emotional stress. The aim of this investigation was to determine the effect of β-endorphin and DSIP on resistance of Wistar and August rats to emotional stress.

EXPERIMENTAL METHOD

Experiments were carried out on 24 adult male Wistar and 25 adult male August rats. Resistance to emotional stress was determined in the animals of each strain by preliminary behavioral open-field testing (tail flick test) in a "Varimex" apparatus, and also by studying the character of changes in the ECG, RVG, blood pressure, and respiration rate in response to stress stimuli [4, 9, 10]. Among the animals studied, in the group of Wistar rats 13 were resistant and 11 predisposed to emotional stress. In the group of August rats 16 were predisposed and 9 resistant to emotional stress. After testing the animals were decapitated and blood and tissue from the hypothalamic regions were taken simultaneously for biochemical testing. Concentrations of immunoreactive β-endorphin-like (β-endorphin) and immunoreactive DSIP-like (DSIP) materials in acetic acid extract of blood and hypothalamus were determined by ELISA. Preliminary treatment of the blood and brain samples was carried out by the usual method [2]. Antiserum to β-endorphin and DSIP was obtained by immunizing rabbits with conjugates of β-endorphin and DSIP with hemocyanin, synthesized with the aid of carbodiimide. β-Endorphin and DSIP conjugates were emulsified in equal volumes of Freund's complete adjuvant and injected subcutaneously and intradermally at a large number of points (up to 100) over the whole body. The animals were reimmunized 2 weeks later with β-endorphin and DSIP conjugate mixed with Freund's incomplete adjuvant. Blood was collected one week after reimmunization. The peptide content was determined in the experimental samples by ELISA, using 96-well polystyrene panels ("Titertek"). To obtain quantitative information, preliminary calibration was carried

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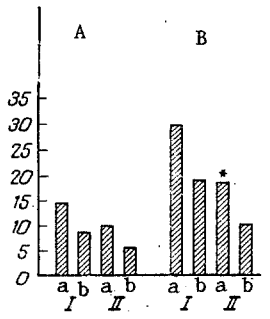

Fig. 1

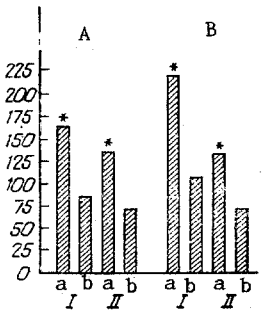

Fig. 2

Fig. 1. Comparison of blood β-endorphin and DSIP levels in Wistar and August rats. I) Rats resistant to emotional stress: a) Wistar (n = 13), b) August (n = 8); II) Rats predisposed to emotional stress: a) Wistar (n = 11), b) August (n = 16). *$p < 0.05$. Ordinate: A) β-endorphin concentration, B) DSIP concentration.

Fig. 2. Comparison of β-endorphin and DSIP levels in hypothalamus of Wistar and August rats. Legend as to Fig. 1.

out against standard solutions of β-endorphin and DSIP. The intensity of the reaction was assessed by means of an MR-580 reader ("Dynatech," Switzerland).

EXPERIMENTAL RESULTS

The experiments revealed differences in the concentrations of β-endorphin and DSIP in the blood and hypothalamus of Wistar and August rats. Furthermore, differences also were observed in the β-endorphin and DSIP concentrations in each of these two strains, which consisted in turn of two groups of animals exhibiting individual resistance to emotional stress. It will be clear from Fig. 1 that in Wistar rats resistant to emotional stress, levels of β-endorphin in the blood and hypothalamus were higher by 59.76 and 93.02%, respectively, than in August rats also resistant to stress. The same pattern also was found with DSIP. The DSIP levels in the blood and hypothalamus of Wistar rats resistant to stress were 63.84% and 47.56%, respectively, higher than in August rats resistant to stress (Fig. 2).

In rats predisposed to stress, β-endorphin levels in the blood and hypothalamus were higher by 66.2% and 91.78%, respectively than in the corresponding August rats. DSIP levels in the blood and hypothalamus were 80.9% and 89.06% higher, respectively, in predisposed Wistar rats.

Within the same genetic strain there were animals which differed in resistance to emotional stress. β-endorphin and DSIP levels also differed in these animals.

For instance, in Wistar rats resistant to emotional stress the β-endorphin levels in the blood and hypothalamus were 44.87% and 21.94% higher, respectively, than in rats of the same strain predisposed to stress. The DSIP levels in the blood and hypothalamus of Wistar rats resistant to stress were 58.52 and 64.3% higher, respectively, than in Wistar rats predisposed to stress.

A similar tendency also was found in August rats. The β-endorphin levels in the blood and hypothalamus of August rats resistant to stress were 43.92% and 21.14% higher, respectively, than in August rats predisposed to emotional stress. DSIP levels in August rats resistant to stress were 82.1% and 47.7% higher in the blood and hypothalamus, respectively, than in rats of the same strain predisposed to emotional stress.

Investigations by several workers have demonstrated differences in neurotransmitter levels in different brain structures of Wistar and August rats, and in the course of emotional stress [1, 3, 11]. Several peptides and, in particular, substance P and enkephalins, have been shown to influence catecholamine turnover [3, 10, 11]. The data cited and the results of the present investigation suggest that β-endorphin and DSIP also participate in the mechanisms of formation of resistance of animals to emotional stress.

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ANTINECROTIC ACTION OF NATURAL AND SYNTHETIC ANTIOXIDANTS IN MYOCARDIAL INFARCTION DUE TO CORONARY OCCLUSION

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Lipid peroxidation (LPO) in mammalian tissue takes place with the participation of antioxidant enzymes, which utilize active forms of oxygen and lipid peroxides (superoxide dismutase, glutathione-dependent lipoperoxidases) and bioantioxidants [4]. Disturbance of the normal regulation of LPO processes in extremal states may lead to the accumulation of toxic lipid peroxidation products in the tissues, which may give rise to oxidation of thiols, inactivation of various enzymes, destruction of biomembranes, and, ultimately, cell death [4]. The writers previously observed a sharp increase in the content of LPO products during ischemic tissue damage [1, 5], the cause of which could be an irreversible decrease in activity of the antioxidative enzymes superoxide dismutase (SOD), glutathione peroxidase (GP), and glutathione-S-transferase [1, 2, 6]. Accordingly, addition of SOD to the cardioplegic solution gives a marked protective effect in myocardial ischemia [13]. Other mechanisms of ischemic tissue damage connected with the accumulation of active forms of oxygen, capable of inducing LPO in biomembranes, also have been discussed in the literature. In particular, a decrease in the oxygen concentration in ischemic cells may lead to an increase in the degree of reduction of pyridine nucleotides, resulting in an increase of the rate of single-electron reduction of oxygen, with the formation of its semireduced form – the superoxide anion-radical [12]. During ischemia proteolytic conversion of xanthine dehydrogenase into xanthine oxidase [12] also takes place, together with stimulation of ATP catabolism, with the accumulation of the substrate of this enzyme (hypoxanthine) [11, 12], and this also promotes an increase in the concentration of active forms of oxygen

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