EFFECT OF β-ENDORPHIN ON SOME ENDOCRINE FUNCTIONS

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Neuropeptides and, in particular, β-endorphins have an extremely broad spectrum of action, one manifestation of which is their participation in the regulation of several endocrine functions [10]. This is particularly true of the trophic functions of the pituitary. The highest concentration of the neuropeptide β-endorphin (compared with other parts of the brain) is found in the region of the arcuate nucleus — median eminence of the hypothalamus, and preoptic-anterior hypothalamic region of the brain, i.e., in the region of the adenohypophyseotrophic zone [14, 20]. Meanwhile, with the aid of suitable reactions, it is possible to demonstrate accumulation of large quantities of monoamines, especially dopamine and noradrenalin, and to a lesser degree serotonin, in the median eminence. Catecholamines are produced by adrenergic neurons, which are numerous in the mediobasal and tuberal parts of the hypothalamus, and they play an important role in regulating the secretion of hypothalamic releasing hormones [1]. There is evidence in the literature that opiate peptides realize their action through modulation of catecholamine neurotransmitter effects [12, 17]. Consequently, close functional connection exists between neuropeptides and the regulatory mechanisms of hypophyseotrophic functions, and this is reflected in the few recent investigations into this problem which, however, have unfortunately dealt mainly with lactotrophic function and have yielded contradictory results [18, 19].

In this investigation an attempt was made to fill this gap by studying blood levels of ACTH, prolactin, thyroid stimulating hormone (TSH), corticosterone, and aldosterone and the pituitary somatotrophin (STH) concentration in rats at different times after administration of β-endorphin.

EXPERIMENTAL METHOD

Experiments were carried out on male rats. β-Endorphin (INC, USA) was injected intravenously (1 ng/kg body weight) and blood was taken from the animals 5, 20, and 60 min later for hormone assay [18]. ACTH, aldosterone, TSH, and prolactin were tested by radioimmunoassay with kits of reagents from Amersham Corporation (England) and CEA-IRE-Sorin (France) respectively; corticosterone was studied by the competitive binding with protein method [2, 3]. Results of TSH and prolactin determination were expressed in relative units, for the binding system used was not homologous. The pituitary STH concentration was determined by dodecylsulfate electrophoresis in polyacrylamide gel. Samples of homogenate were prepared and electrophoretic separation of the samples carried out by the method in [5].

EXPERIMENTAL RESULTS

β-endorphin has a marked effect on secretion of ACTH, prolactin, corticosterone, and aldosterone and on STH formation in the pituitary (Table 1). The maximal increase in concentration of these hormones occurred after 20 min, although an increase in the concentration of some of them was observed as early as 5 min after injection. This agrees with data published by other workers [18] and is evidence that the terminal $t_{1/2}$ of β-endorphin is 16-30 min.

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TABLE 1. Blood ACTH, TSH, Prolactin, Corticosterone, and Aldosterone Levels and STH Concentration in Adenohypophysis of Rats at Different Times after Injection of β-Endorphin

Experimental conditions	ACTH, ng/ml	TSH, ng/ml	Prolactin, ng/ml	STH, μg/mg	Corticosterone, μg/100 ml	Aldosterone, ng/ml
Control (n = 10)	164±20	1,3±0,8	17,67±3,50	44,75±5,9	12,3±1,5	25,5±1,4
After injection of β-endorphin:						
5 min (*n*=10)	428,5±12,0	1,08±0,6	25,7±4,8	42,0±3,7	18,0±1,2	47,2±3,7
P	<0,001	>0,5	>0,1	>0,5	<0,01	<0,001
20 min (*n*=10)	645±20	1,21±0,5	56,7±5,5	68,75±4,4	27,0±2,3	94,0±5,1
P	<0,001	0,2	<0,001	<0,01	<0,001	<0,001
60 min (*n*=10)	405±17	1,1±0,51	17,7±2,4	39,7±3,7	10,0±1,9	22,75±2,20
P	<0,001	>0,5	>0,5	>0,2	>0,2	>0,2

Legend. P) Significant relative to control.

The results of investigation of the pituitary—adrenal system showed that the blood ACTH level, which was significantly raised 5 min after injection of β-endorphin, continued to rise until the 20th minute, but was lower after 60 min, although it did not reach the control values. At the same time similar changes were observed in the blood corticosterone and aldosterone concentrations, more marked in the latter case. The blood corticosterone and aldosterone levels of the rats 60 min after injection of β-endorphin had fallen to the level characteristic of intact animals, but the ACTH concentration was increased.

Investigation of the blood prolactin level and STH concentration in the adenohypophysis of rats after injection of β-endorphin showed a significant increase at the 20th minute with a return to the control level after 1 h. No statistically significant changes in the concentrations of these hormones were observed 5 min after injection of β-endorphin (Table 1). β-endorphin had no effect on the blood TSH level.

It can be concluded that β-endorphin has a considerable influence on processes controlling secretion and, perhaps, synthesis of pituitary hormones (ACTH, STH, prolactin) by stimulating these functions of the pituitary. One of the probable mechanisms lying at the basis of the action of β-endorphin on the secretion of these hormones is through changes in the relative concentrations of brain monoamines (especially dopamine), which function as a connecting link between the CNS and secretory neurons controlling the secretion of the pituitary trophic hormones under study [7, 16].

Some investigators have in fact shown that β-endorphin leads to a marked reduction in the synthesis and turnover of dopamine and inhibits its release from hypothalamic neurons [11]. This in turn induces secretion of prolactin releasing hormone and, correspondingly, the secretion of prolactin by pituitary cells [12], as is shown by values obtained for the blood prolactin level in the early stages after injection of β-endorphin in the present experiments. Changes in the ratio of biogenic amines in the hypothalamus under the influence of β-endorphin (a fall of the dopamine level for 20-25 min) can serve to explain the high STH concentration in the pituitary of rats receiving β-endorphin [11, 17-19]. The increase in the blood ACTH concentration of rats after injection of β-endorphin also is due to some degree to a decrease in the dopamine concentration in the brain under the influence of β-endorphin and consequent stimulation of formation of corticotrophin releasing factor [6]. We have shown that injection of β-endorphin, which has a marked stimulating effect on secretion of ACTH, STH, and prolactin, evidently as a result of lowering the brain dopamine concentration, has virtually no effect on the thyrotrophic function of the pituitary. This is probably due to the fact that dopaminergic structures play a negligible part in the regulation of thyrotrophin function [4].

The view that opioid peptides regulate several pituitary functions by modulating effects of catecholamines, especially dopamine, is confirmed by the results of investigations in which, besides β-endorphin or morphine, blockers of opiate or dopamine receptors (naloxone, haloperidol, or the dopamine antagonist bromocriptine, were injected [8, 11].

In the course of the study of mechanisms controlling lactotrophic function the authors concerned put forward the hypothesis, which they extended to other pituitary trophic functions,

that β-endorphin is involved in these processes at the hypothalamic level, and with specific releasing hormones. However, these workers do not rule out the possibility that β-endorphin exerts its influence directly at the pituitary level, where opiate receptors have been identified [9, 18].

In a study of the effect of β-endorphin on function of the pituitary–adrenal system, the present writers showed that 5 and 20 min after its injection changes of identical direction are observed in the ACTH, corticosterone, and aldosterone levels. After 60 min, however, when the blood ACTH level still remains quite high, almost the same as after 5 min, the gluco- and mineralocorticoid levels have fallen to their values in intact rats. Such a reduction in the adrenocortical response to ACTH can be explained, first, by the presence of a definite decrease in this reaction to repeated activation of the adrenal tissue by ACTH. It is considered that changes in the adreno-cortical reaction of this kind may be due not only to ACTH [15].

Second, the absence of an adrenal response of rats after injection of β-endorphin, despite a high ACTH level, may be due to the direct stimulating action of the neuropeptide on adrenal tissue and the considerable weakening of this effect after 60 min because of the fall in the blood β-endorphin concentration [13].

LITERATURE CITED

1. B. V. Aleshin, Usp. Fiziol. Nauk, No. 1, 48 (1974).
2. A. F. Bunyatyan, A. G. Volchek, and V. B. Rozen, Probl. Éndokrinol., No. 3, 36 (1975).
3. A. G. Volchek, Nauch. Dokl. Vyssh. Shkoly, Biol. Nauki, No. 10, 124 (1973).
4. E. M. Stabrovskii, A. S. Egorkova, L. S. Shpanskaya, et al., Probl. Éndokrinol., No. 2, 62 (1981).
5. I. N. Shostak, O. T. Rozhko, and F. P. Martynenko, Vopr. Med. Khim., No. 1, 71 (1980).
6. M. F. Dallman, J. Physiol. (Paris), 77, 951 (1982).
7. J. Farah, D. Malcolm, and G. Mueller, Endocrinology, 110, 657 (1982).
8. A. Guidotti and L. Grandison, in: Endorphins in Mental Health Research, E. Usedin, et al., eds., New York (1979), pp. 416-426.
9. B. Kerdelhul, C. Bethea, N. Ling, et al., Brain Res., 231, 85 (1982).
10. E. Costa and M. Trabucchi, The Endorphins, Raven Press, New York (1978).
11. G. Loon, D. Ho, and C. Kim, Endocrinology, 106, 76 (1980).
12. J. Meites, J. Bruni, D. Van Vugt, et al., Life Sci., 24, 1325 (1979).
13. K. Racz, E. Glaz, R. Kiss, et al., Biochem. Biophys. Res. Commun., 97, 1346 (1980).
14. M. Sar, W. Stumpf, R. Miller, et al., J. Comp. Neurol., 182, 17 (1978).
15. E. B. De Soura and G. R. van Loon, Endocrinology, 110, 23 (1982).
16. S. Spampinato, V. Locatelli, L. Cocci, et al., Endocrinology, 105, 163 (1979).
17. D. A. Van Vugt and J. Meites, Fed. Proc., 39, 2533 (1980).
18. S. L. Wardlaw, W. Wehrenberg, M. Ferin, et al., Endocrinology, 107, 1663 (1980).
19. W. Wehrenberg, D. McNicol, S. L. Wardlaw, et al., Endocrinology, 109, 544 (1981).
20. M. Wilkes, W. Watkins, R. Stewart, et al., Neuroendocrinology, 30, 113 (1980).