EFFECT OF SHOCK FOLLOWING PROLONGED CRUSHING OF SOFT TISSUES ON HYPOTHALAMIC-PITUITARY-ADRENAL FUNCTION

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The corticotropin-releasing activity of the hypothalamus (CRF), the ACTH content in the pituitary, and the ascorbic acid content in the adrenals were studied in acute experiments on rats at various times during shock accompanying the prolonged crush syndrome. At the beginning of crushing (a pressure of 6 atm over a surface of 12.2 cm^2) the CRF and ACTH levels rose. After crushing for 4 h the CRF activity was restored, the ACTH content reached its maximum, and the ascorbic acid content fell. The CRF activity and ACTH and ascorbic acid content were much reduced 3 h after decompression.

Prolonged crushing of the soft tissues stimulates adrenal [3-6] and pituitary [6, 9] function considerably. The mechanism of involvement of the pituitary-adrenal system in the pathogenesis of shock in general [11] and of the crush syndrome in particular, is not yet clear. In the modern view, the formation and secretion of ACTH are under the control of hypothalamic corticotropin-releasing factor (CRF) [16, 17, 19, 20]. The action of a stressor can induce phasic changes in CRF [1] and ACTH [10] activity. Morphological changes in the hypothalamus in certain types of shock are evidence of changes in neurosecretory processes [2, 7, 8]. However, specific components of the hypothalamic neurosecretion cannot be detected by morphological methods.

The object of this investigation was to study the state of hypothalamic-pituitary-adrenal (HPA) function in the shock period of the prolonged crush syndrome (PCS).

EXPERIMENTAL METHOD

Experiments were carried out on 170 noninbred male albino rats. The PCS was induced by crushing the soft tissues by compression by means of a combined press and manometer of the author's design, under constant manometric control. The intensity of compression was 6 atm on a surface of 12.2 cm^2 on both sides of the animals (total load 73.2 kg for 4 h). In each series of experiments (control, after compression for 5 and 10 min and 4 h, and after decompression for 3 h) the animals were decapitated and the following determinations carried out: hypothalamic CRF activity by testing hypothalamic extract on recipient animals [1, 14], the ACTH content in the pituitary by testing on recipient animals [12, 15], and the ascorbic acid content in the adrenals [18].

EXPERIMENTAL RESULTS

It will be clear from Table 1 that hypothalamic CRF activity, the ACTH content in the pituitary, and the ascorbic acid content in the adrenals of the intact rats in these experiments agreed with data in the literature [1, 12]. Crushing the soft tissues gave rise during the first minutes to a sharp increase in hypothalamic CRF activity and an equally large increase in the ACTH level in the adenohypophysis, but the change in the ascorbic acid concentration in the adrenals at this time was less marked. Consequently, in the first stage of the acute crush syndrome CRF was produced or liberated from its cell depots extremely rapidly and accumulated in the hypothalamus. Synthesis and liberation of releasing factor are known to

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TABLE 1. CRF Activity of Hypothalamic Extracts, ACTH Content in Pituitary, and Ascorbic Acid Content in Adrenals of Rats at Various Periods of PCS (M ± m)

Series of experiments	No. of expts.	Hypothalamic			Pituitary ACTH			Adrenal ascorbic acid		
		decrease in ascorbic acid (mg %)	%	P≤	i.u./100 μg acetone-treated tissue	%	P≤	mg %	%	P≤
Intact rats	10	135±38	100		7,8±0,3	100		423±10	100	
Compression, 5 min	8	204±25	151	0,2	14,0±0,5	180	0,01	345±10	82	0,001
Compression, 10 min	16	319±32	235	0,001	22,8±2,5	290	0,001	319±25	75	0,01
Compression, 4h	14	107±28	80	0,5	37,5±5,0	480	0,001	226±23	53	0,001
Decompression	14	28±11	20	0,02	4,0±0,8	51	0,001	156±19	37	0,001

take place simultaneously, with synthesis predominating over liberation [13]. Meanwhile CRF was also probably excreted, for there was a parallel increase in the liberation, formation, and accumulation of ACTH as the result of hypothalamic activation.

During prolonged crushing for several hours these relations in HPA activity were altered. After the end of compression for 4 h the CRF activity was down to its initial level but the ACTH content was at a maximum and the ascorbic acid content in the adrenals was much lower. The restoration of CRF activity toward the end of compression can be interpreted as the continuation of hypothalamic activation during which the liberation of CRF exceeded its formation. ACTH synthesis in the pituitary at this stage was evidently increased more than is apparent from the table, for considerable quantities of it were discharged at the same time into the general circulation (activation of the adrenal glands, reflected in their increased ascorbic acid level).

In the decompression stage of the shock period of the PCS, hypothalamic CRF activity and the content of ACTH in the pituitary and of ascorbic acid in the adrenals all fell considerably. The decrease in CRF activity and in the ACTH level was evidently the result of the exhaustion of their reserves in the hypothalamus and pituitary because of the great excess of liberation over their formation in the decompression stage. Evidence in support of this view is given by maintenance of the high level of adrenal function. The possibility likewise cannot be ruled out that the decrease in CRF activity and in the ACTH content may be linked with the commencing exhaustion of the formation of these biologically active substances. Morphological changes in hypothalamic neurosecretion in the PCS similarly occur in phases [8].

In PCS the activities of the various components of the HPA system thus reach their maximum at different times, in the following order: hypothalamus (maximum after compression for 10 min), pituitary (maximum at the end of compression), and adrenals (maximum at the end of the observations).

LITERATURE CITED

1. I. A. Drzhevetskaya and A. D. Borodin, Pat. Fiziol., No. 3, 42 (1971).
2. S. A. Eremina and E. S. Gul'yants, in: Mechanisms of Some Pathological Processes [in Russian], No. 2, Rostov-on-Don (1968), p. 336.
3. M. I. Kuzin et al., Ortoped. Travmatol., No. 11, 70 (1967).
4. V. K. Kulagin, The Role of the Adrenal Cortex in the Pathogenesis of Trauma and Shock [in Russian], Leningrad (1965).
5. L. T. Lysyi, in: Neuro-Humoral Disturbance in Trauma [in Russian], No. 2, Kishinev (1968), p. 126.
6. G. S. Mazurkevich, The Role of the Pituitary-Adrenal Systems in the Pathogenesis of Traumatic Shock, Candidate's Dissertation [in Russian], Leningrad (1967).
7. L. I. Muzykant and V. F. Gordeev, Éksper. Khir., No. 4, 42 (1969).
8. A. K. Mulatova and G. Kh. Kardash'yan, in: Mechanisms of Some Pathological Processes [in Russian], No. 4, Rostov-on-Don (1971), p. 35.
9. A. I. Robu, in: Neuro-Humoral Disturbances in Trauma [in Russian], No. 2, Kishniev . (1968), p. 183.
10. V. M. Rozental', in: The Physiology, Biochemistry, and Pathology of the Endocrine System [in Russian], Kiev (1969), p. 28.

11. B. A. Saakov and S. A. Eremina, in: Mechanisms of Some Pathological Processes [in Russian], No. 2, Rostov-on-Don (1968), p. 215.
12. Yu. B. Skebel'skaya, Probl. Endokrinol., No. 5, 74 (1964).
13. N. A. Yudaev and Z. F. Evtikhina, in: Current Problems in Endocrinology [in Russian], Moscow No. 4 (1972), p. 8.
14. A. Arimura, T. Saito, and A. Schally, Endocrinology, 81, 235 (1967).
15. M. K. Birmingham et al., Endocrinology, 59, 677 (1956).
16. R. Guillemin, in: The Investigation of Hypothalamic-Pituitary-Adrenal Function, Cambridge (1968), p. 19.
17. K. Lissak and E. Endröczi, Neuro-Endocrine Regulation of Adaptive Activity [in Russian], Budapest (1967).
18. J. H. Roe and C. A. Kuether, J. Biol. Chem., 147, 399 (1943).
19. M. Saffran and A. Schally, Endocrinology, 57, 439 (1955).
20. J. Szentagothai et al., Hypothalamic Regulation of the Anterior Pituitary [in Russian], Budapest (1965).