52. IS THE NORMAL CIRCADIAN RHYTHM OF CORTISOL PRESERVED IN PATIENTS DURING PROLONGED COMA?

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It is generally accepted that the primary modulator of the circadian rhythm of cortisol secretion resides in the central nervous system. Our aim was to investigate whether the normal circadian periodicity of cortisol secretion is preserved in patients during prolonged coma. Blood samples were taken at 08.00, 16.00, 24.00, 08.00 from 14 male and 4 female patients (age: 7-50 years) in coma for periods ranging from 6 weeks to 6 years due to corticocerebral injury or anoxia. Of the 18 patients studied, only 6 succeeded in satisfying the criteria of a normal circadian rhythm in cortisol: 08.00 cortisol level equal to, or greater than, twice the level at 24.00, and level at 24.00 equal to, or less than, 6 μg/dl serum. In several patients the test was repeated on more than one occasion and the same result was obtained. The presence or lack of a normal circadian periodicity in cortisol was not related to age, sex, etiology or duration of coma, and may be dependent on the location and degree of the lesion.

53. STIMULATION OF RAT ADRENOCORTICAL TISSUE REQUIRES PROTEOLYTIC ACTIVITY

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In zona glomerulosa preparations addition of the trypsin inhibitor Nα-p-tosyl-L-arginine methyl ester (TAME, 10mM) inhibits the response of 11-deoxycorticosterone (DOC), corticosterone (B), 18-hydroxycorticosterone (18-OH-B), 18-hydroxydeoxycorticosterone (18-OH-DOC), and aldosterone (aldo) to ACTH (10^{-7}M) and K^+ (8.4mM) in whole capsules in vitro, and to ACTH, Angiotensin II and αMSH (all at 10^{-7}M) in collagenase-dispersed glomerulosa cells. TAME (10mM) also prevented the normal ACTH-induced rise in cAMP output from collagenase-dispersed glomerulosa cells. In contrast to results with ACTH or K^+, TAME (10mM) had no effect on the cAMP stimulated output of B or 18-OH-DOC, but 18-OH-B and aldo were inhibited (both $p<0.001$). This selective inhibitory action on 18-OH-B and aldo is also seen in K^+, ACTH and cAMP stimulated whole capsules on the addition of the αchymotrypsin active site titrant 2-nitro-4-carboxyphenyl-N-N'-diphenylcarbamate (NCDC, 2μM). It is concluded that proteolytic enzymes are involved at two stages in the response to acute stimulation of the rat zona glomerulosa (i) at a site prior to cAMP generation and (ii) in the specific release of 18-OH-B and aldo. This second site of action may be the release of steroid from the recently-described novel steroid-protein complexes. (Raven,P.W. et al, 1982, BBRC, 104, (4), 1247-1254).

54. 18-Hydroxycorticosterone (18-OH-B) in Hypercortisolism

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The formation of 18-hydroxycorticosterone (18-OH-B) in hypercortisolism was studied. Elevated 18-OH-B excretions were found in 2 of 4 patients with Cushing's disease due to an adrenal adenoma, in 2 of 8 patients with ACTH dependent Cushing's disease (1 of them with ectopic ACTH-syndrome) and in 1 of 3 patients with adrenal carcinoma. In some asthma bronchiale patients treated for 7 days with supraphysiological doses of ACTH the 18-OH-B values were elevated, while others remained in the normal range. Elevated values of aldosterone-18-glucuronide in the patients with Cushing's disease were found only exceptionally and not in the patients with elevated 18-OH-B. After ACTH treatment the aldosterone-18-glucuronide values were low. The results indicate that under certain conditions 18-OH-B may be synthesized by the zona fasciculata of the adrenal cortex.