In vitro cAMP, aldosterone and cortisol responses of adult human adrenocortical tissue to ACTH and human growth hormone

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Summary. The acute in vitro effects of ACTH and HGH in human adrenals were examined. HGH acts synergistically with ACTH in augmenting adrenal aldosterone output. This effect is not due to cAMP alterations in response to HGH. HGH slightly depresses the human adrenal cortisol response to ACTH.

Rat adrenals rapidly and specifically bind ^{125}I-HGH, an effect enhanced by ACTH[1,2]. Uptake occurs in all 3 adrenocortical zones, but appears most intense in the zona glomerulosa[1]. This is consistent with the reported GH enhancement of aldosterone secretion by rat adrenals[3,4]. Further, growth hormone increases corticosterone production in the adrenals of hypophysectomized rats in response to ACTH[4–7]. These effects are believed to be at least partially mediated by a reduction of adrenal microsomal 5 α-reductase activity[5,8]. In addition to the steroidogenic effects, growth hormone increases mitotic activity in the hypophysectomized rat adrenal[9]. The studies to date have provided evidence to support the hypothesis that GH is a modulator of adrenal function. However, these investigations have examined growth hormone effects at comparatively long time intervals post stimulations (h to days). In the present communication we describe the effects of HGH and ACTH on human adrenal cAMP and steroid output during short term (min) in vitro incubations.

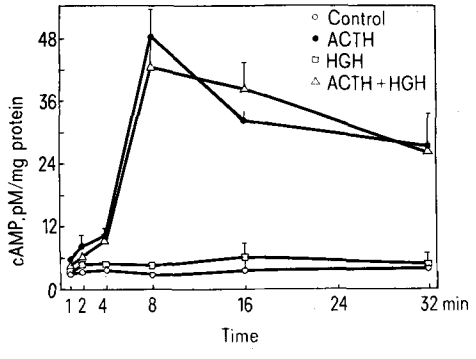

Fig. 1. Temporal cAMP response to HGH, ACTH and ACTH + HGH compared to controls. Vertical bars indicate SEM. Lack of vertical bar indicates that the SEM is smaller than the symbol.

Materials and methods. 3 adult human female adrenal glands obtained at surgery were immediately placed in cold (0–4 °C) Krebs' Ringer bicarbonate buffer, KRBGA (pH 7.4, 200 mg glucose/dl, 0.5% serum albumin fraction V). Glands were diced (2×3 mm) and preincubated (37 °C) in KRBGA for 45 min. These dice then were incubated (1 ml KRBGA; 37 °C; 95% O_2 + 5% CO_2) in a Dubnoff metabolic shaker for 1–32 min. The dice were exposed to porcine ACTH (100 mIU/ml; chromatographically pure; 150 IU/mg), HGH (1 μg/ml; NIH-GH-HS1394) or KRBGA alone. Further, dice were incubated initially (4 min) in ACTH, followed by transfer to ACTH + HGH. Adrenal incubates were quenched in liquid nitrogen and analyzed for cAMP by RIA[10]. Cortisol and aldosterone secretion into the incubation medium was quantitated by RIA[11,12]. Proteins were determined[13] and the data expressed as pM cAMP or ng steroid/mg protein, $\bar{X} \pm$ SEM. A minimum of 3 tissue replicates were used per datum point. Data were analyzed by analysis of variance and Student's t-test. Differences were accepted as significant when $p < 0.05$.

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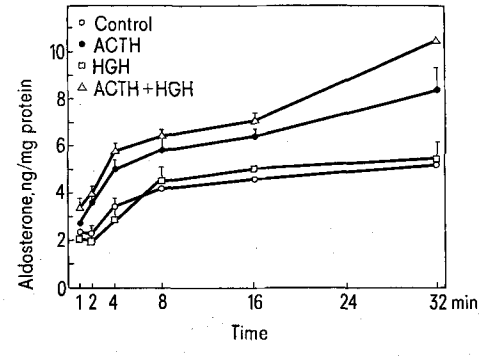

Fig. 2. Temporal aldosterone response to HGH, ACTH and ACTH + HGH compared to controls. Vertical bars indicate SEM. Lack of vertical bar indicates that the SEM is smaller than the symbol.

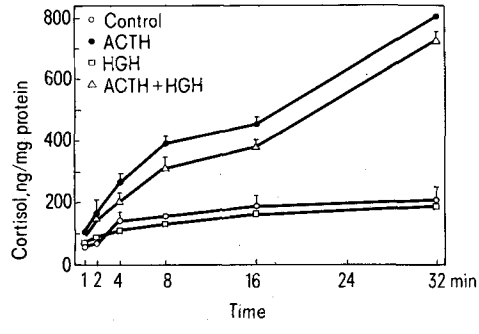

Fig. 3. Temporal cortisol response to HGH, ACTH and ACTH + HGH compared to controls. Vertical bars indicate SEM. Lack of vertical bar indicates that the SEM is smaller than the symbol.

Results and discussion. The cAMP levels in the control adrenal incubates were low (4.7 ± 0.58) and not significantly different at the time intervals studied (figure 1). ACTH significantly increased (2 min) human adrenal cAMP above control levels with a peak response at 8 min (figure 1). This response is typical of that observed in other mammalian adrenals[14]. HGH alone did not alter cAMP levels from that of the controls (figure 1). The combined effects of ACTH plus HGH were not different from those of ACTH alone (figure 1). HGH, therefore, does not appear to modulate basal or ACTH stimulated adrenocortical cAMP[15,16].

A slow basal aldosterone output during the period of study was demonstrated in the control groups (figure 2). This short term basal aldosterone output was not significantly affected by HGH. However, ACTH significantly increased aldosterone output by 4 min (figure 2). ACTH + HGH significantly increased aldosterone output above that of ACTH alone at 32 min (figure 2). This agrees with the findings in the rat adrenal[4-7].

The cortisol levels of the control and HGH groups were not significantly different (figure 3). A gradual increase in this basal cortisol output occurred in both groups during the 32 min interval studied. ACTH significantly increased cortisol output within 2 min; a continuous cortisol rise occurred during the 32 min incubation period (figure 3). Growth hormone acts synergistically with ACTH to increase corticosterone output by rat adrenals[5]. However, ACTH + HGH resulted in significantly lower human adrenal cortisol output at 32 min (figure 3). This variance may be the result of inherent species differences. Nevertheless, more fundamentally, these results may indicate an effect of GH at the level of microsomal 17 α-hydroxylase activity. Inhibition at this point would shunt steroidogenesis toward mineralocorticoid production with a resultant increase in both corticosterone and aldosterone production as observed in the rat[4-7]. However, as the rat does not produce cortisol, the depressed output of this steroid observed in the human adrenal has not been previously reported. Interestingly, GH increases aldosterone production in response to ACTH in both the rat and human adrenal. GH has been demonstrated in inhibit some adrenal enzyme activity (5 α-reductase)[5-8]. The present suggestion may add yet another site for GH modulation of adrenal steroidogenesis.

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Effets comparatifs de JH-I et de JH-II chez Locusta migratoria L.

Differential effects of JH-I and JH-II on Locusta migratoria L.

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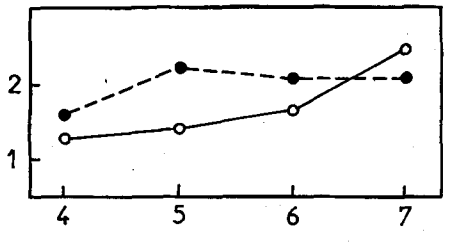
Summary. Study of differential effects of JH-I and JH-II on metamorphosis, pigmentation and oocytes maturation shows evidence for a more specific action of JH-I in controlling metamorphosis.

Depuis la mise en évidence de 3 hormones juvéniles chez les insectes[1-4]; de nombreux travaux ont été consacrés à leur activité biologique. Cependant, et bien qu'il semble que ces hormones soient présentes en quantité d'ailleurs variables, chez le même insecte[5-7], où elles pourraient avoir des fonctions différentes, très peu d'études ont été entreprises pour comparer leur effet différentiel sur les fonctions de l'insecte et tendre à déterminer l'hormone la plus apte à contrôler la métamorphose, la maturation ovarienne, etc.[8]. C'est cette lacune que nous tentons de combler en ce qui concerne Locusta migratoria.



Action de 10 µg de JH-I (○) ou de JH-II (●) sur la taille des ovocytes de femelles privées de corpora allata au jour 1 de la vie imaginale. Ordonnée: longueur des ovocytes en mm; abscisse: jours après l'injection des hormones; n = 5 pour chaque point.

Matériel et méthodes. Nous étudions les effets comparatifs des hormones juvéniles en C_{16} (JH-I) et C_{17} (JH-II) sur la métamorphose, la pigmentation et la maturation ovarienne chez le Criquet migrateur africain, en phase grégaire. Les composés chimiques, qui proviennent des Laboratoires Calbiochem, sont des substances racémiques présentant la stéréoisomérie des hormones naturelles.

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