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Chemical and Restraint-induced Modulation of Pro-opiomelanocortin in the Skin.

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The interaction between stress-induced activation of the hypothalamic-pituitary-adrenal axis (HPAA) and the immune system is well established. Several researchers have localized many components of the HPAA in the skin, including corticotropin releasing hormone receptor, pro-opiomelanocortin (POMC), adrenocorticotropic hormone and alpha-melanocorticotropin, and have postulated the existence of a cutaneous HPAA. To determine if the cutaneous HPAA is activated in development of contact dermatitis, epidermal sheets from C57BL/6 mice were incubated for 20 minutes in 1X PBS alone or 1X PBS containing 10μg/ml phorbol myristyl acetate (PMA) or 0.25% dinitrochlorobenzene (DNCB) dissolved (4:1) in acetone/olive oil, and POMC expression was evaluated by RT-PCR. Low constitutive expression of POMC in unstimulated epidermal sheets was significantly increased by PMA and DNCB. Dexamethasone (1×10^{-8} M), a negative regulator of POMC expression, blocked constitutive expression and chemical-induced expression of POMC. To determine if restraint stress alters cutaneous expression of POMC *in vivo*, mice were restrained for two hours prior to application of vehicle, PMA, or DNCB to the ear, and expression of POMC was visualized by *in situ hybridization*. Restraint increased serum corticosterone from 30.9 ± 15 pg/ml to 582.4 ± 16 pg/ml, indirect verification of activation of the HPAA. Minimal expression of POMC was visualized in vehicle-treated skin for both non-restrained and restrained mice. A significant increase in the number of POMC-positive epidermal cells was observed for PMA and DNCB, and, restraint stress further increased the number of positively stained cells. These data demonstrate increased expression of cutaneous POMC in response to chemical and to restraint which can be downregulated by synthetic glucocorticoids.