S-2 Membrane Receptors for Steroid Hormones Explain Rapid Responses to Corticosterone.

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The well-established model for the mechanism of action for steroid hormones involves intracellular receptors that act as transcription factors regulating gene expression. Recent research reveals that, in addition to this genomic action, steroid hormones can exert actions through other mechanisms, including signal transduction by cell-surface receptors. One example of this alternative mechanism comes from neuroendocrine investigations in the roughskin newt (*Taricha granulosa*). In this amphibian, corticosterone rapidly and potently inhibits reproductive behaviors by binding to a novel class of corticosteroid receptors in neuronal membranes. Elevated corticosterone concentrations in Taricha, either due to exogenous administration or normal physiological stress responses, suppress male clasping behavior within minutes. There is a high-affinity binding site for corticosterone in neuronal membranes(K_d=0.5 nM) with characteristics of a bona fide receptor. It also has unique pharmacological specificity(with low or modest affinities for many Type I and II ligands) and appears to be physiologically relevant for controlling rapid behavioral responses to stress. Negative modulation of this receptor by guanyl nucleotide suggests that it may use signal transduction mechanisms associated with guanine nucleotide-binding proteins. Other evidence also indicates that, although other steroids can modulate the $GABA_A$ receptor, this corticosteroid receptor is distinct from steroid-recognition sites on the $GABA_A$ receptor. In neurophysiological studies, corticosterone administration produces multiple neuro-physiological effects, as in non-reticulospinal neurons that show a rapidly-developing decline or cessation of spontaneous firing and depression of sensory responsiveness, especially to pressure(a clasp-eliciting stimulus in sexually active males). These neuro- physiological responses are specific to corticosterone; administration of dexa- methasone, which binds poorly to the membrane rece-ptor and does not affect reproductive behavior, has little or no direct neurophysiological effect on medullary neurons. These studies all support the conclusions that the rapid inhibition of behavior by corticosterone involves corticosteroid receptors in neuronal membranes and the suppression of neuronal processing of specific sensory information.