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Dehydroepiandrosterone: Cellular mechanisms modulating aggression 1

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Dehydroepiandrosterone (DHEA) is a neuroactive neurosteroid, the most abundant steroid in humans, and is available as an over-the-counter dietary supplement. A diverse array of biological and behavioral effects have been attributed to DHEA, with one of the most well established being the inhibition of female-typical aggression when given chronically. The mechanism of action underlying this inhibition, however, remains an open question. Previous models had held that DHEA exerted its anti-aggressive (and other behavioral) effects strictly through modulation of cell surface receptors. More recently, however, it was shown that DHEA, either directly or through androgenic metabolites, exerted genomic effects through the androgen receptor (AR). This presentation will review *in vitro* and *in vivo* studies that characterize neurobiological effects of DHEA on GABA-A receptor, a major target implicated in the inhibition of aggression, and on AR function in the CNS, including intracellular trafficking and gene regulation. A model that integrates these signaling functions with the modulation of aggression in response to extended DHEA treatment will be proposed.

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