DHEA-S AND PREGNENOLONE MAY PROTECT THE BRAIN FROM DEMENTIA AND ALZHEIMER'S DISEASE

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Some neurosteroids have been shown to display beneficial effects on neuroprotection in rodents. To investigate the physiopathological significance of neurosteroids in Alzheimer's disease (AD), we compared the concentrations of pregnenolone, pregnenolone sulfate (PREGS), dehydroepiandrosterone, dehydroepiandrosterone sulfate (DHEAS), progesterone, and allopregnanolone, measured by gas chromatography-mass spectrometry, in individual brain regions of AD patients and aged nondemented controls, including hippocampus, amygdala, frontal cortex, striatum, hypothalamus, and cerebellum. A general trend toward decreased levels of all steroids was observed in all AD patients' brain regions compared with controls: PREGS and DHEAS were significantly lower in the striatum and cerebellum, and DHEAS was also significantly reduced in the hypothalamus. A significant negative correlation was found between the levels of cortical beta-amyloid peptides and those of PREGS in the striatum and cerebellum and between the levels of phosphorylated tau proteins and DHEAS in the hypothalamus. This study provides reference values for steroid concentrations determined by gas chromatography-mass spectrometry in various regions of the aged human brain. High levels of key proteins implicated in the formation of plaques and neurofibrillary tangles were correlated with decreased brain levels of PREGS and DHEAS, suggesting a possible neuroprotective role of these neurosteroids in AD.