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The neurosteroid allopregnanolone is reduced in prefrontal cortex in Alzheimer's disease

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Abstract

Background: Few data are currently available investigating neurosteroids (NS) in Alzheimer's disease (AD). The NS allopregnanolone may be decreased in serum and plasma in patients with AD, but it is unclear if allopregnanolone is also reduced in brain. Because a number of NS exhibit neuroprotective effects and impact cognitive performance in rodent models, these molecules may be relevant to the pathophysiology of neurodegenerative disorders. We therefore investigated prefrontal cortex (PFC) NS levels in AD.

Methods: Neurosteroid levels (allopregnanolone, pregnenolone, dehydroepiandrosterone [DHEA]) were determined in postmortem PFC in 14 male subjects with AD and 15 cognitively intact male control subjects by gas chromatography/mass spectrometry preceded by high-performance liquid chromatography purification.

Results: Subjects with AD exhibit significant reductions in allopregnanolone compared with cognitively intact control subjects (median levels = 2.50 ng/g vs. 5.59 ng/g, respectively; p = .02). Allopregnanolone levels are inversely correlated with neuropathological disease stage (Braak), r = -.49, p = .007. Median DHEA levels are elevated in subjects with AD (p = .01).

Conclusions: Subjects with AD demonstrate significant reductions in PFC allopregnanolone levels, a finding that may be relevant to neuropathological disease stage severity. Neurosteroids may have utility as candidate biomarkers in AD.

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