

# Androgen therapy may slow progress of Alzheimer's disease

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Experiments on mouse models of Alzheimer's disease (AD) suggest that treatment with male sex hormones might slow its progression. The findings, published in the December 20 issue of *The Journal of Neuroscience*, provide new insight into the relationship between testosterone loss and AD, which affects 4.5 million Americans.

Senior author Christian Pike, PhD, of the University of Southern California (USC), with colleagues at USC and the University of California, Irvine, sought to better understand the role hormones play in aging and disease. Recent studies had already established a link between testosterone loss in men and AD due to natural aging.

The research team established a correlation between low testosterone and elevated beta-amyloid (A $\beta$ ), a protein that accumulates abnormally in AD patients. This finding, they say, suggests that testosterone depletion in aging men may be a risk factor for AD by promoting accumulation of A $\beta$  in the brain. Testosterone, the primary male sex hormone, is one in a group of related steroid hormones referred to as androgens. Recent studies suggest that androgens may lower A $\beta$  levels.

"This study raises the possibility that androgen replacement therapy might lower the risk for Alzheimer's, but this is far from proven," says Sam Gandy, MD, PhD, chair of the Alzheimer's Association's Medical and Scientific Advisory Council and director of the Farber Institute for Neurosciences at Thomas Jefferson University. "Because testosterone is rapidly converted to estrogen after entry into neurons, the new data are

logical, and they dovetail well with historical data."

Using a mouse model of AD, in which three genes had been altered, researchers evaluated how experimental manipulation of sex hormones affected the progress of the disease. Researchers removed the testes of young adult male mice and over several months, treated some with a testosterone hormone and others with a placebo.

After the treatment period, memory-related behavior and measures of Alzheimer-like pathology were measured in the different groups of mice. The castrated models that received the placebo showed poor working memory and high brain levels of A $\beta$ . However, both A $\beta$  accumulation and cognitive decline were prevented in mice treated with the hormone therapy.

"Although the results of the study predict that androgen therapy has the potential to reduce the risk of AD in at least some men," Pike said, "clinical studies will be required to determine when and how to use androgen therapy."

Source: Society for Neuroscience

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