

## TESTOSTERONE AND ESTROGEN MAY HELP PREVENT ALZHEIMER'S DISEASE

Testosterone changes the processing of beta-amyloid precursor protein towards a harmless or even beneficial form of beta-amyloid peptide ("beta-amyloid precursor protein alpha") and away from the form associated with Alzheimer's disease ("beta-amyloid peptides"), according to new research from The Rockefeller University in New York City.

According to an author of the recently published research, Dr. Paul Greengard, testosterone directs brain metabolism so that much beta-amyloid precursor protein so that more goes to the good pathway and much less to the bad pathway.

In the February 1st issue of Proceedings of the National Academy of Sciences, Dr. Greengard and colleagues report on experiments in which they added testosterone to either rat neuroblastoma cells containing the gene for human beta-amyloid precursor protein or primary rat neurons.

In rat neuroblastoma cells, they found that testosterone caused a 50% to 75% increase in the levels soluble beta-amyloid precursor protein-alpha, which is harmless to neurons, and a 30% to 45% decrease in the levels of amyloid beta peptides found in Alzheimer's disease. Treatment with estrogen produced similar results, and similar results were also obtained in primary rat neurons.

In contrast, treatment with cholesterol led to an increase in the secretion of beta-amyloid peptides with no effect on the secretion of soluble beta-amyloid precursor protein-alpha, while treatment with the corticosterone had no effect on the secretion of either protein.

"In older men and in older women, there's a decrease in the level of testosterone, so the thought is that one might do some trials of testosterone in aging men to see whether it would reduce the incidence of Alzheimer's disease as

estrogen appears to do in women," according to Dr. Greengard "In addition, since women need both estrogen and testosterone, instead of just using estrogen in the treatment of postmenopausal women, the thought is to try to combine estrogen and testosterone."

Other laboratories have found in preliminary work that the results showing the increase in secreted beta-amyloid precursor protein alpha and the decrease in beta-amyloid peptides after estrogen or testosterone treatment occurs in intact animals.

Dr. Greengard's laboratory is currently studying how estrogen and testosterone affect processing of beta-amyloid precursor protein. Early results suggest that these hormones might also speed the passage of beta-amyloid precursor protein through the cell, leaving less time for proteases (enzymes which break down proteins) to gain access to the protein and degrade it to the harmful beta-amyloid peptides.

**Gouras GK, Xu H, Gross RS, Greenfield JP, Hai B, Wang R, Greengard P.**

***Testosterone reduces neuronal secretion of***

***Alzheimer's beta-amyloid peptides. Proc Natl Acad Sci U S A. 2000 Feb 1;97(3):1202-5.***