

# Is There Less Alzheimer's Disease Neuropathology in Medicated Elderly Hypertensives?

## Background and Importance

Epidemiological studies over the past two decades indicate that people with hypertension in middle age have a greater risk of developing Alzheimer Disease (AD) later in life. It is clearly advantageous to know if intervention with currently available medications can reduce future brain damage in those with established hypertension. Several clinical research groups have investigated whether treatment of hypertension reduces the risk of later AD, but findings have been inconsistent. We feel that these inconsistencies may have resulted from inherent weaknesses of clinical studies. As noted, the various clinical methods available differ importantly in their ability to identify individuals with dementia. Current clinical tools are also untrustworthy in diagnosing the specific dementia. At the Jewish Home (JHH) we have the advantage of detailed, recorded clinical observations of our residents, and a longstanding autopsy program that has allowed expert neuropathological studies of about 500 of our residents over the past 22 years. This provides us with the opportunity to study the brains of residents who had had hypertension—both treated and untreated—as well as residents who had not had hypertension in their lifetime.

## Objectives

Using detailed neuropathological study, to test the hypothesis that use of antihypertensive medication is associated with reduction of AD brain pathology.

## Methods

In collaboration with the NIH-supported Alzheimer Study Group at Mount Sinai School of Medicine, we have compiled a large database with detailed information from postmortem studies and clinical charts of about 500 JHH residents. From this database, we excluded those with any dementing neuropathology other than AD, and also those with AD plus other neuropathology. The remaining 291 residents are included in our study. They have been grouped as: (1) those without hypertension during life (No-HTN; n=172); (2) those with clinically recorded hypertension but no record of treatment (HTN-nomed; n=42); and (3) those with clinically recorded hypertension who had received anti-hypertensive medication (HTN-med; n=77). Medical and demographic information for each has been derived from JHH records. Brains have undergone intensive study by a small team of expert neuropathologists, following the protocol established by the

Consortium to Establish a Registry for Alzheimer's Disease (CERAD). This includes detailed counting of neuritic plaques (NP) and neurofibrillary tangles (NFT) in each brain region pertinent to AD. Utilizing one-way analyses of variance (ANOVA), HTN-med, HTN-nomed and No-HTN groups are compared for the frequencies of NP and NFT in multiple regions of the brain.

Sets of 24 neuropathological analyses are assessed using the Holm procedure to control for multiple comparisons. The data are adjusted for several covariates: age of death, gender, presence of an ApoE4 allele and BMI.

### **Current status**

The statistical evaluation of extensive information is continuing. Results to date are of great interest: it appears that medicated hypertensive residents (HTN-med) had significantly less neuropathology than untreated hypertensive (HTN-nomed) or even of non-hypertensives (No-HTN). These findings are strongly suggestive of a protective affect of antihypertensive medication against AD-associated neuropathology.

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**Funded by:** National Institute on Aging (NIA)  
Dextra Baldwin McGonagle Foundation  
Joseph E. and Norma G. Saul Foundation

**Project Period:** 2008-2011

### **Publications**

Hoffman, L.B, Schmeidler, J., Lesser, G. T., Beeri, M. S. Purohit, Haroutunian, V. (2009). Less Alzheimer's disease neuropathology in medicated elderly hypertensives than in non hypertensives. *Neurology*, 72, 1720-26.

Updated: June 2010